# WEST Search History

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DATE: Wednesday, June 21, 2006

| Hide? | Set Name | Query | Hit Count |
|---|---|---|---|
| | *DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ* | | |
| ☐ | L8 | (L7 and TAA) | 9 |
| ☐ | L7 | (L6 and (dendritic adj cell)) | 57 |
| ☐ | L6 | (L4 and (APC or dc)) | 67 |
| ☐ | L5 | (L4 and (cancer adj grade)) | 1 |
| ☐ | L4 | (L3 and (fusion adj protein)) | 85 |
| ☐ | L3 | (L2 and prostate) | 115 |
| ☐ | L2 | (L1 and (prostatic acid phosphatase)) | 136 |
| ☐ | L1 | (pap and (gm adj csf) and cancer) | 996 |

END OF SEARCH HISTORY

- Search History will be lost after eight hours of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.
- Click on query # to add to strategy



| Search | Most Recent Queries | Time | Result |
|---|---|---|---|
| #24 | Search **prostatic acid phosphatase and GM-CSF** | 12:41:55 | 9 |
| #23 | Search **pap and (gm-csf) and adrenal** | 12:41:20 | 0 |
| #22 | Search **pap and (gm-csf) and pancreas** | 12:41:12 | 0 |
| #21 | Search **pap and (gm-csf) and ovary** | 12:41:06 | 0 |
| #20 | Search **pap and (gm-csf) and stomach** | 12:41:00 | 0 |
| #19 | Search **pap and (gm-csf) and rectum** | 12:40:53 | 0 |
| #18 | Search **pap and (gm-csf) and colon** | 12:40:47 | 0 |
| #17 | Search **pap and (gm-csf) and larynx** | 12:40:40 | 0 |
| #15 | Search **pap and (gm-csf) and breast** | 12:39:49 | 2 |
| #14 | Search **pap and (gm-csf) and bladder** | 12:39:37 | 0 |
| #13 | Search **pap and (gm-csf) and endometrium** | 12:39:28 | 0 |
| #11 | Search **pap and (gm-csf) and lung** | 12:39:02 | 47 |
| #12 | Search **pap and (gm-csf) and lung and phosphatase** | 12:38:53 | 0 |
| #10 | Search **pap and (gm-csf) and bone** | 12:37:37 | 8 |
| #9 | Search **pap and (gm-csf) and cervix** | 12:37:30 | 0 |
| #8 | Search **pap and (gm-csf) and uterine** | 12:37:23 | 0 |
| #7 | Search **pap and (gm-csf) and esophagus** | 12:37:12 | 0 |
| #6 | Search **pap and (gm-csf) and brain** | 12:36:49 | 1 |
| #4 | Search **pap and (gm-csf) and lymphoma** | 12:35:59 | 2 |
| #3 | Search **pap and (gm-csf) and sarcoma** | 12:35:14 | 1 |
| #2 | Search **pap and (gm-csf) and prostate** | 12:34:42 | 7 |
| #1 | Search **pap and (gmcsf) and prostate** | 12:34:35 | 6 |

Clear History

Jun 14 2006 10:29:54

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| | | |
|---|---|---|
| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | | "Ask CAS" for self-help around the clock |
| NEWS 3 | JAN 17 | Pre-1988 INPI data added to MARPAT |
| NEWS 4 | FEB 21 | STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results |
| NEWS 5 | FEB 22 | The IPC thesaurus added to additional patent databases on STN |
| NEWS 6 | FEB 22 | Updates in EPFULL; IPC 8 enhancements added |
| NEWS 7 | FEB 27 | New STN AnaVist pricing effective March 1, 2006 |
| NEWS 8 | MAR 03 | Updates in PATDPA; addition of IPC 8 data without attributes |
| NEWS 9 | MAR 22 | EMBASE is now updated on a daily basis |
| NEWS 10 | APR 03 | New IPC 8 fields and IPC thesaurus added to PATDPAFULL |
| NEWS 11 | APR 03 | Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL |
| NEWS 12 | APR 04 | STN AnaVist $500 visualization usage credit offered |
| NEWS 13 | APR 12 | LINSPEC, learning database for INSPEC, reloaded and enhanced |
| NEWS 14 | APR 12 | Improved structure highlighting in FQHIT and QHIT display in MARPAT |
| NEWS 15 | APR 12 | Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected |
| NEWS 16 | MAY 10 | CA/CAplus enhanced with 1900-1906 U.S. patent records |
| NEWS 17 | MAY 11 | KOREAPAT updates resume |
| NEWS 18 | MAY 19 | Derwent World Patents Index to be reloaded and enhanced |
| NEWS 19 | MAY 30 | IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2 |
| NEWS 20 | MAY 30 | The F-Term thesaurus is now available in CA/CAplus |
| NEWS 21 | JUN 02 | The first reclassification of IPC codes now complete in INPADOC |

NEWS EXPRESS JUNE 16 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 23 MAY 2006.

| | |
|---|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |
| NEWS X25 | X.25 communication option no longer available after June 2006 |

Enter NEWS followed by the item number or name to see news on that specific topic.



* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

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FILE 'HOME' ENTERED AT 11:57:08 ON 21 JUN 2006

=> file caplus, bioeng, biotechno, biotechds, esbiobase
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY    SESSION
FULL ESTIMATED COST                             0.21       0.21

FILE 'CAPLUS' ENTERED AT 11:57:29 ON 21 JUN 2006
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=> s (pap and gm (w) csf) and cancer)
UNMATCHED RIGHT PARENTHESIS 'CANCER)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (pap and (gm (w) csf) and cancer)
L1          31 (PAP AND (GM (W) CSF) AND CANCER)

=> duplicate remove l1
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L1
L2           25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)

=> s (l2 and prostate)
L3          17 (L2 AND PROSTATE)

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L3
L4           17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 11:57:08 ON 21 JUN 2006)

     FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
     11:57:29 ON 21 JUN 2006
L1           31 S (PAP AND (GM (W) CSF) AND CANCER)
L2           25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L3           17 S (L2 AND PROSTATE)
L4           17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d l4 bib abs 1-17

L4   ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2005:1321617  CAPLUS
TI   Safety and immunological efficacy of a prostate cancer
     plasmid DNA vaccine encoding prostatic acid phosphatase (PAP)
```

AU Johnson, Laura E.; Frye, Thomas P.; Arnot, Alana R.; Marquette, Carrie; Couture, Larry A.; Gendron-Fitzpatrick, Annette; McNeel, Douglas G.
CS Department of Medicine, Section of Medical Oncology, K4/518 Clinical Science Center, University of Wisconsin-Madison, Madison, WI, 53792, USA
SO Vaccine (2006), 24(3), 293-303
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier B.V.
DT Journal
LA English
AB Prostatic acid phosphatase (**PAP**) is a **prostate** tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clin. benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat **PAP** can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunol. efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human **PAP**, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-wk intervals with 100, 500, or 1500 μg pTVG-HP with 5 μg recombinant rat **GM-CSF** protein given as a vaccine adjuvant. An addnl. 12 male Lewis rats served as controls with groups immunized with 1500 μg of a parental DNA vector not encoding human **PAP**, and a group that received **GM-CSF** protein only without plasmid DNA. Groups of animals (n = 3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunol. anal. No significant toxicities were observed in terms of animal wts., histopathol., hematol. changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically different from control animals. The vaccine was found to be effective in eliciting **PAP**-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and nos. of immunizations. **PAP**-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting **PAP**-specific cellular and humoral immune responses. These findings support the further clin. evaluation of pTVG-HP in patients with **prostate cancer**.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:72938 CAPLUS
TI Provenge: **prostate cancer** therapy
AU McIntyre, J. A.; Fernandez, D.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2005), 30(9), 892-895
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. There are few therapeutic options available for the treatment of hormone-refractory **prostate cancer** (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing **prostate**-specific T-cell-mediated immunity. Provenge (APC-8015) is an immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (**PAP**), an antigen found in 95% of **prostate cancers**, and granulocyte-macrophage colony-stimulating factor (**GM-CSF**). Early clin. studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge, with increases in **prostate**

-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1127402 CAPLUS
DN 142:54751
TI Alternative reading frame peptides as antigens for the prophylaxis and treatment of **cancer** and infectious diseases
IN Graddis, Thomas; Laus, Reiner; Diegel, Michael; Vidovic, Damis
PA Dendreon Corporation, USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004111075 | A2 | 20041223 | WO 2004-US6979 | 20040305 |
| | WO 2004111075 | C1 | 20050519 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2514288 | AA | 20041223 | CA 2004-2514288 | 20040305 |
| | US 2005112134 | A1 | 20050526 | US 2004-794514 | 20040305 |
| | EP 1601684 | A2 | 20051207 | EP 2004-749357 | 20040305 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| PRAI | US 2003-453131P | P | 20030305 | | |
| | WO 2004-US6979 | W | 20040305 | | |

AB Alternative reading frame (ARF) peptides associated with disease conditions and that can be recognized by antigen presenting cells (APC) and dendritic cells (DC) are described for use as antigens in the diagnosis, treatment, and prevention of diseases including **cancer** and infectious diseases. These peptides may arise from frameshifting, use of alternative start codons, ribosomal skipping, suppression of termination of translation, translation of antisense transcripts, splice variants or use of cryptic promoters. Alternative reading frame peptides derived from the HER-2 receptor gene were incubated with mouse dendritic cells in vitro and the cells reintroduced into the donor mice. Mice challenged with B16 cells blocked tumor growth, whereas animals treated with inframe HER-2 proteins did not.

L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:287861 CAPLUS
DN 140:320038
TI Chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation
IN Goldenberg, David M.; Hansen, Hans; Leung, Shui-on
PA Immunomedics, Inc., USA; Mccall, John Douglas
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004029093 | A2 | 20040408 | WO 2003-GB4229 | 20030930 |
| | WO 2004029093 | A3 | 20040603 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CN 1542019 | A | 20041103 | CN 2003-123054 | 20030429 |
| | CA 2500250 | AA | 20040408 | CA 2003-2500250 | 20030930 |
| | AU 2003269225 | A1 | 20040419 | AU 2003-269225 | 20030930 |
| | EP 1546204 | A2 | 20050629 | EP 2003-751001 | 20030930 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRAI | US 2002-414341P | P | 20020930 | | |
| | WO 2003-GB4229 | W | 20030930 | | |

AB The present invention provides humanized, chimeric and human MN3 antibodies, fusion proteins, and fragments that bind NCA90 and NCA95 antigens. The antibodies, fusion proteins, and fragments thereof, as well as combinations with other suitable antibodies, are useful for the treatment and diagnosis of granulocyte related disorders and diseases, such as leukemia.

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:270002 CAPLUS
DN 140:302326
TI Immunotherapeutic compositions comprising antigen presenting cells (APCs) stimulated by fusion proteins (such as APC binding protein fused to tumor-associated antigen), and use of compositions in treatment of moderately to well-differentiated **cancers**
IN Laus, Reiner; Gold, Mitchell; Madhusudan, Peshwa; Pickering, Grant; Kylstra, Jelle; Peshwa, Madhusudan
PA Dendreon Corporation, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004026238 | A2 | 20040401 | WO 2003-US29176 | 20030919 |
| | WO 2004026238 | C1 | 20040722 | | |
| | WO 2004026238 | A3 | 20041209 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2497554 | AA | 20040401 | CA 2003-2497554 | 20030919 |
| | AU 2003267254 | A1 | 20040408 | AU 2003-267254 | 20030919 |

US 2004161413 A1 20040819 US 2003-666122 20030919
EP 1540627 A2 20050615 EP 2003-749725 20030919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-412271P P 20020920
US 2003-475355P P 20030602
US 2003-475335P P 20030602
WO 2003-US29176 W 20030919
AB The invention discloses immunotherapeutic compns. comprising activated antigen presenting cells (APCs), wherein said APCs were obtained from **cancer** patients and stimulated by exposure ex vivo to a fusion protein composed of a APC binding protein and tumor-associated (specific) antigen. The invention also discloses the use of said stimulated/activated APCs in treatment of patients with moderately to well-differentiated **cancer** cells. The invention further provides a method of assessing in **cancer** patients the susceptibility of **cancer** to said immunotherapeutic compns. As way of illustration, the invention discloses a fusion protein (APC8015) composed of a portion of **prostate** tumor-associated protein human prostatic acid phosphatase (huPAP) at the N-terminus and a portion of APC/DC binding protein human granulocyte-macrophage colony stimulating factor (huGM-CSF) at the C-terminus. APC stimulated by exposure ex vivo to said **PAP/GM-CSF** fusion protein were effective in activating T cells to produce a cytotoxic cellular response against huPAP. Finally, the invention discloses the amino acid sequences of huPAP and huGM-CSF. In the examples, the invention demonstrated that the therapeutic efficacy of immunotherapeutic compns. comprising APCs stimulated with **PAP/GM-CSF** fusion protein correlates with the differentiation state of the **prostate cancer** cells. Specifically, it was demonstrated that patients exhibiting moderately to well-differentiated prostrate **cancer** cells were susceptible to treatment with said immunotherapeutic composition The invention also demonstrated the efficacy of a combined immunotherapeutic treatment regimen that includes administration of **PAP/GM-CSF**-pulsed dendritic cells in conjunction with administration of humanized anti-VEGF monoclonal antibody Bevacizumab in patients having a serol. progression of **prostate cancer**.

L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:589231 CAPLUS
DN 141:134058
TI Methods and compositions for treating **prostate cancer** using DNA vaccines
IN McNeel, Douglas
PA Wisconsin Alumni Research Foundation, USA
SO U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004142890 | A1 | 20040722 | US 2003-669474 | 20030925 |

PRAI US 2002-413777P P 20020927
AB A DNA vaccine for the treatment of **prostate cancer**, comprising a plasmid vector comprising a nucleotide sequence encoding prostatic acid phosphatase (**PAP**) operably linked to a transcription regulatory element, wherein upon administration to a mammal a cytotoxic immune reaction against cells expressing **PAP** is induced. In preferred embodiment, the **PAP** encoded is a xenoantigen highly homologous to the autoantigen **PAP** of the mammal. Also disclosed are methods for inducing prostatitis, or inducing immune reaction to **PAP**, or treating **prostate**

**cancer** in a mammal, using the DNA vaccine and pharmaceutical compns. comprising the vaccine. Preferably, xenoantigen vaccination is followed by boosting with autoantigen **PAP** from the same animal species as the mammal being treated. Lewis rats immunized with pTVG-HP, encoding human **PAP**, developed **PAP**-specific cellular immunity and **prostate** tissue inflammation.

L4 ANSWER 7 OF 17 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-21964 BIOTECHDS
TI Treating **cancer** with an immunotherapeutic composition comprises determining differentiation state of **cancer** cells, where presence of moderately to well-differentiated cells indicates patient susceptible to treatment with the composition;
composition for **cancer** immunotherapy comprises dendrite cell exposed to tumor-associated antigen
AU LAUS R; GOLD M H; PESHWA M; PICKERING G; KYLSTRA J
PA DENDREON CORP
PI US 2004161413 19 Aug 2004
AI US 2003-666122 19 Sep 2003
PRAI US 2003-666122 19 Sep 2003; US 2002-412271 20 Sep 2002
DT Patent
LA English
OS WPI: 2004-614827 [59]
AN 2004-21964 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Treating (M1) a **cancer** patient with an immunotherapeutic composition where the patient has a **cancer** with moderately to well-differentiated **cancer** cells, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment with an immunotherapeutic composition, and administering the composition, where a reduction of 10% indicates an effective treatment of the **cancer**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an immunotherapeutic composition (I) comprising activated, isolated antigen presenting cells (APCs) that are obtained from a patient diagnosed with a **cancer** having a moderate to well-differentiated **cancer** grade and are stimulated by exposure ex vivo to a tumor-associated antigen (TAA); (2) inhibiting (M2) growth of a **cancer** cell in a patient having a moderate to well differentiated **cancer** grade, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment, isolating APCs from the patient, stimulating the APCs by exposure ex vivo to the immunotherapeutic composition comprising a protein conjugate having an N-terminal moiety and a C-terminal moiety, where the APCs are effective to activate T-cells to produce a cytotoxic cellular response against either the N-terminal moiety or the C-terminal moiety and where the level of the T-cell activation is higher than that produced by the APCs when exposed exclusively to the N- or C-terminal moiety, and administering to the patient the stimulated APCs, where a reduction of 10% indicates an effective treatment of the **cancer** and (3) a method of assessing in a **cancer** patient the susceptibility of the **cancer** to an immunotherapeutic composition, comprising isolating from the patient a sample containing the **cancer** cell, and determining the differentiation state of the **cancer** cell, where a moderate to well differentiated **cancer** grade indicates that the **cancer** is susceptible to treatment with an immunotherapeutic composition.

WIDER DISCLOSURE - Also disclosed are nucleic acids, polypeptides, host cells, vectors and antibodies used in the methods of the invention.

BIOTECHNOLOGY - Preferred Method: The composition is (I). Preferred

Composition: The TAA of the immunotherapeutic composition is a tumor-specific antigen, or is a component of a protein conjugate comprising an N- and C-terminal moiety. The APCs are dendritic cells. The **cancer** is soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or **prostate**. The **cancer** grade corresponds to a Gleason score of at most 7. The patient is not refractory to hormone ablation therapy. The N- or C-terminal moiety is an APC binding protein an/or a TAA. The fusion protein further comprises, between the N- and the C-terminal moiety, a linker peptide. The N- or C-terminal comprises a sequence having at least 70, 80, 90 or 100% identical to huPAP or huGM-CSF with a fully defined sequence of 386 or 144 amino acids (SEQ ID NO: 1 and 3), respectively, as given in the specification.

ACTIVITY - Cytostatic; Immunostimulant. Prior to initiating an immunotherapeutic treatment regimen with **PAP/GM-CSF** fusion protein (APC8015) or placebo, patients were assessed for baseline disease characteristics. To determine the differentiation state of **prostate cancer** cells, **prostate** tissue samples were isolated from each patient and subjected to analysis by the Gleason scoring methodology as described in Gleason, Urologic Pathology: The **Prostate**, pp. 171-197 (Tappenhaum, ed., Lee and Fehiger, Philadelphia, Pa., 1977). Time to objective disease progression was defined as progression on bone scan or x-ray or clinical deterioration and the data were subjected to statistical analysis by the Kaplan-Meier methodology. PSA was not used to determine disease progression. The median time to disease progression for the patient population treated with APC8015 was 11.0 weeks whereas the median time to disease progression for the patient population treated with placebo was 9.1 weeks. The data demonstrated that patients having poorly differentiated **prostate cancer** cells were refractory to treatment with APC8015 as evidenced by the absence of a statistically significant difference (p-value=0.431) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo. In contrast, the results obtained for patients exhibiting moderately to well-differentiated **prostate cancer** cells (having a Gleason score of less than or equal to 7) show that such patients were susceptible to treatment with an immunotherapeutic composition as evidenced by the high degree of statistical significance (p-value=0.002) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo.

MECHANISM OF ACTION - None given.

USE - For treating **cancers** including soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or **prostate** (claimed).

ADMINISTRATION - Routes of administration of the pharmaceutical compositions include oral, pulmonary, intramuscular, intraperitoneal, intravenous, subcutaneous, inhalation, transdermal, nasal, vaginal, rectal and sublingual. No dosages given.

ADVANTAGE - The method is based upon the observation that the grade of a **cancer** cell, being a measure of the cell's differentiation state, is predictive of clinical outcome in **cancer** patients undergoing an immunotherapeutic treatment regimen. Whereas poorly differentiated cells were found to be refractory to an immunotherapeutic treatment regimen, moderately to well-differentiated cells were highly susceptible to treatment with immunotherapeutic compositions. (34 pages)

L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:715711 CAPLUS
DN 141:294358
TI Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can

induce durable remission of metastatic androgen-independent **prostate cancer**: a phase 2 trial

AU Burch, Patrick A.; Croghan, Gary A.; Gastineau, Dennis A.; Jones, Lori A.; Kaur, Judith S.; Kylstra, Jelle W.; Richardson, Ronald L.; Valone, Frank H.; Vuk-Pavlovic, Stanimir

CS Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, MN, USA

SO Prostate (New York, NY, United States) (2004), 60(3), 197-204
CODEN: PRSTDS; ISSN: 0270-4137

PB Wiley-Liss, Inc.

DT Journal

LA English

AB **Prostate cancer** is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (**PAP**) and **GM-CSF**. We enrolled 21 patients with histol. documented androgen-independent **prostate** carcinoma that could be evaluated by radionuclide bone scan or computed tomog. scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-pos. PA2024-loaded APCs with admixts. of monocytes, macrophages, B and T cells. APC8015 was infused i.v. twice, 2 wk apart. Two weeks after the second infusion, patients received three s.c. injections of 1.0 mg of PA2024 1 mo apart. We monitored patients' phys. condition, immune response, and laboratory parameters. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in **prostate**-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/mL at baseline to undetectable levels by week 24 and has remained so for more than 4 yr. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 wk proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 wk. This study demonstrates a definite clin. response of androgen-independent **prostate cancer** to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:719518 CAPLUS

DN 139:259962

TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and conjugates for diagnosis and treatment of **cancer**

IN Govindan, Serengulam; Qu, Zhengxing; Hansen, Hans J.; Goldenberg, David M.

PA Immunomedics, Inc., USA; Mccall, John Douglas

SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003074566 | A2 | 20030912 | WO 2003-GB885 | 20030303 |
| | WO 2003074566 | A3 | 20040304 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| CA 2478047 | AA | 20030912 | CA 2003-2478047 | 20030303 |
| AU 2003209447 | A1 | 20030916 | AU 2003-209447 | 20030303 |
| US 2004001825 | A1 | 20040101 | US 2003-377121 | 20030303 |
| EP 1483295 | A2 | 20041208 | EP 2003-743420 | 20030303 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1649903 | A | 20050803 | CN 2003-809918 | 20030303 |
| JP 2006502698 | T2 | 20060126 | JP 2003-573031 | 20030303 |
| PRAI US 2002-360229P | P | 20020301 | | |
| WO 2003-GB885 | W | 20030303 | | |

AB This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in a host. More specifically, the present invention relates to the tumor-associated antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

L4 ANSWER 10 OF 17 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2003:37239077 BIOTECHNO
TI Cell therapy and **prostate cancer**
THERAPIE CELLULAIRE ET **CANCER** DE LA **PROSTATE**
AU Eymard J.-C.; Bernard J.
CS J.-C. Eymard, U. Fonct. Rech. Clin./Therapie Cell., Institut Jean-Godinot, 1, av. du gen. Koenig, 51056 Reims Cedex, France.
E-mail: jc.eymard@reims.fnclcc.fr
SO Bulletin du Cancer, (2003), 90/8-9 (734-743), 63 reference(s)
CODEN: BUCABS ISSN: 0007-4551
DT Journal; General Review
CY France
LA French
SL English; French
AB Hormonotherapy is the standard treatment for advanced **prostate cancer** but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of **cancer** cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use **GM-CSF** gene-transduced allogenic cells.
The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two **prostate** antigens have already been used, PSMA evaluated in 130 patients and a fusion protein **PAP-GM-CSF** (Provenge®) in 144 patients.
All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to

amplify vaccine response and clinical efficacy.

L4 ANSWER 11 OF 17 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2005226190 ESBIOBASE
TI Session II: Tumor antigens - **Prostate cancer** antigens and vaccines
AU Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.; Belldegrun A.; Logothetis C.; Papandreou C.
CS Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA, United States.
SO Cancer Immunology, Immunotherapy, (2003), 52/SUPPL. 1 (S8-S9+S27) CODEN: CIIMDN ISSN: 0340-7004
DT Journal; Conference Article
CY Germany, Federal Republic of
LA English
SL English
AB The clinical development of **prostate cancer** vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those **cancers** for which tumor and immune cells are readily available. Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory **prostate cancer** (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of **prostate cancer**: **prostate**-specific membrane antigen (PSMA), **prostate**-specific antigen (PSA), and prostatic acid phosphatase (**PAP**). Following conclusive preclinical evidence indicating that the human body responds immunologically to **prostate** antigens, clinical trials have been underway for many years with PSMA, PSA, and **PAP** as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (**GM-CSF**, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due

to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. .COPYRGT. 2002 Northwest Biotherapeutics, Inc. All rights reserved.

L4 ANSWER 12 OF 17 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-15068 BIOTECHDS
TI Eliciting or enhancing immune response to human self tumor antigen e.g. HER-2/neu protein for preventing tumor occurrence by immunizing individual with foreign protein or its portion homologous to the self antigen;
recombinant vaccine against **cancer**
AU CHEEVER M A; DISIS M L
PA CHEEVER M A; DISIS M L
PI US 2002019331 14 Feb 2002
AI US 1996-88951 1 Apr 1996
PRAI US 1998-88951 2 Jun 1998
DT Patent
LA English
OS WPI: 2002-303155 [34]
AN 2002-15068 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Eliciting or enhancing an immune response to a human self tumor antigen involves immunizing a human being with a foreign protein homologous to the antigen or with a foreign peptide homologous to a portion of the antigen.

BIOTECHNOLOGY - Preferred Method: The foreign protein or peptide is present in a carrier or diluent. The method additionally involves the use of an adjuvant.

ACTIVITY - Antitumor.

MECHANISM OF ACTION - Immune response enhancer or elicitor (claimed). Rats (Fischer strain 344 (CDF (F-344)/CrIBR)) were immunized with recombinant human HER-2/neu intracellular domain protein (hICD) (50 microg) or immunoaffinity column purified rat neu protein (50 microg). Proteins were administered with either complete Fruend's antigen (CFA) or murine granulocyte macrophage-colony stimulating factor (**GM-CSF**) 5 microg as adjuvants. Control groups received adjuvant alone. Animals underwent immunizations each 14-16 days apart. 18-10 days after the second immunizations animals were assessed for immunologic response. Rats immunized with hICD developed high titer human and rat neu specific antibodies. All rats immunized with hICD developed significant antibody responses specific for human HER-2/neu protein, with titers greater than 1:200,000. Human HER-2/neu ICD is 92% homologous to rat neu ICD at the amino acid level. Analysis was performed to discern whether the human HER-2/neu specific antibodies were cross-reactive with rat neu. Rats immunized with hICD with either **GM-CSF** or CFA as an adjuvant had high titer antibody responses specific for rat neu. The magnitude of the rat neu specific antibody responses was nearly identical to that of the human HER-2/neu specific response. Delayed type hypersensitivity (DTH) responses were used to initially evaluate for the presence of the T cell responses to neu in rats immunized with HER-2/neu. HER-2/neu specific DTH responses were detected in animals who received hICD in **GM-CSF** or CFA. The responses were cross-reactive to rat neu protein. DTH was not detected in animals immunized with rat neu protein or with adjuvants alone. Immunization of rats with hICD elicits detectable T cell responses specific for both human and rat neu protein. T cell proliferative responses were evaluated in rats immunized with hICD plus either **GM-CSF** or CFA. T cell responses to hICD protein were detected from lymph nodes draining the inoculation site. T cell responses to rat neu protein were also detected, although at a lower magnitude than the hICD response.

USE - For eliciting or enhancing an immune response to a human self tumor antigen which a protein expression product of an over expressed human oncogene such as HER-2/neu protein, or a portion of the human HER-2/neu protein, where the portion includes the intracellular domain of

the human HER-2/neu protein. Optionally the immune response is elicited or enhanced against an antigen or antigen portion which is an organ-specific or tissue-specific differentiation antigen associated with tumor cells, or a portion of the antigen. Preferably the organ- or tissue-specific differentiation antigen is an antigen associated with **prostate cancer**, e.g. prostatic acid phosphatase ( **PAP**) or **prostate** specific antigen (PSA) (all claimed).
The method is useful for eliciting or enhancing an immune response as a preventing measure to prevent tumor occurrence or recurrence, or as therapy to arrest tumor growth or eradicate existence tumors or to prolong the survival.

ADMINISTRATION - The vaccine composition is administered by intradermal, subcutaneous or intravenous routes. Dosages range from 1 microg/kg-1 mg/kg, preferably 5-200 microg/kg.

ADVANTAGE - The method overcomes immunological tolerance which exists and represents a potential barrier to effectively vaccinating against human self tumor antigens, by immunizing an individual with a protein or peptide that is foreign (i.e., not identical to that in the individual) but nevertheless homologous to an individuals self tumor antigen or its portion. (26 pages)

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:417000 CAPLUS
DN 135:32745
TI Antigen-binding fragments specific for tumor associated antigens
IN Dan, Michael; Entwistle, Joycelyn; Fast, Darren; Kaplan, Howard; Lewis, Keith; MacDonald, Glen; Maiti, Pradip
PA Novopharm Biotech Inc., Can.
SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001040292 | A1 | 20010607 | WO 1999-CA1141 | 19991129 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI WO 1999-CA1141 19991129
AB The present invention relates to antigen-binding fragments that are specific for stress protein-peptide complexes specifically associated with tumors, particularly human tumors, and compns. thereof. The compns. are suitable for diagnostic and pharmaceutical use. The invention further provides methods of making and screening for the antigen-binding fragments. The invention further encompasses compns. containing **cancer**-associated stress protein-peptide complexes (including derivs. thereof) and methods of use thereof. The **cancer**-specific stress protein-peptide complexes (SPPC's) are particularly useful in eliciting **cancer**-specific immunogenic responses against a plurality of **cancers**. The invention also provides novel phage display libraries for use in producing further SPPCs and anti-SPPCs of the invention.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:224352 CAPLUS

DN 134:251211
TI Monoclonal antibody to C-antigen: Prophylaxis and detection of **cancer**
IN Dan, Michael D.; Maiti, Pradip K.; Kaplan, Howard A.
PA Viventia Biotech, Inc., Can.
SO U.S., 56 pp., Cont.-in-part of U.S. Ser. No. 657,449, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6207153 | B1 | 20010327 | US 1997-862124 | 19970522 |
| | CA 2255540 | AA | 19971127 | CA 1997-2255540 | 19970522 |
| | CN 1229436 | A | 19990922 | CN 1997-194815 | 19970522 |
| | NZ 505305 | A | 20020628 | NZ 1997-505305 | 19970522 |
| | KR 2000015893 | A | 20000315 | KR 1998-709444 | 19981121 |
| | AU 775448 | B2 | 20040729 | AU 2000-72432 | 20001220 |
| | US 2003021779 | A1 | 20030130 | US 2001-782397 | 20010213 |
| | US 2004091484 | A1 | 20040513 | US 2003-651453 | 20030829 |
| PRAI | US 1996-657449 | B2 | 19960522 | | |
| | AU 1997-33696 | A3 | 19970522 | | |
| | NZ 1997-332566 | A1 | 19970522 | | |
| | US 1997-862124 | A1 | 19970522 | | |
| | US 2001-782397 | B1 | 20010213 | | |

AB The authors disclose preparation and sequence characterization of monoclonal antibody H11 that specifically binds to an antigen (termed "C-antigen") expressed by diverse tumors and tumor cell lines. The C-antigen was not found on normal cells. Also disclosed are polynucleotides and single chain antibodies based on H11 for application in therapy and tumor imaging.
RE.CNT 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:869162 CAPLUS
DN 142:233296
TI Consensus peptide presenting entities, screening methods, and use for the treatment and diagnosis of tumors.
IN Maiti, Pradip K.; Herman, William; Dan, Michael D.; Kaplan, Howard A.; MacDonald, Glen C.; Entwistle, Jocelyn M.; Lewis, Keith E.; Fast, Darren G.
PA Novopharm Biotech Inc., Can.
SO Can. Pat. Appl., 155 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | CA 2290722 | AA | 20010608 | CA 1999-2290722 | 19991208 |
| PRAI | CA 1999-2290722 | | 19991208 | | |

AB The invention provides antigen-binding-fragments specific for tumor cells and effective in treatment and/or diagnosing tumors. Methods of use are also provided as are methods for screening for addnl. such antigen-binding-fragments and the products obtained thereby.

L4 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:445203 CAPLUS
DN 133:87934
TI Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for **prostate cancer**
AU Burch, Patrick A.; Breen, Jami K.; Buckner, Jan C.; Gastineau, Dennis A.; Kaur, Judith A.; Laus, Reiner L.; Padley, Douglas J.; Peshwa, Madhusudan

V.; Pitot, Henry C.; Richardson, Ronald L.; Smits, Bouwien J.; Sopapan, Pitsata; Strang, George; Valone, Frank H.; Vuk-Pavlovic, Stanimir

CS Divisions of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905, USA

SO Clinical Cancer Research (2000), 6(6), 2175-2182
CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB We attempted to induce therapeutic immunity against **prostate** -derived tissues in patients suffering from progressive hormone-refractory metastatic **prostate** carcinoma. Thirteen patients were treated with two infusions, 1 mo apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (**GM-CSF** ) and human prostatic acid phosphatase (**PAP**). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating **prostate**-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by **GM-CSF** ($P = 0.0004$) and **PAP** ($P = 0.0001$), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against **PAP** and **GM-CSF**. However, antibodies to **GM-CSF** and, to a much lesser extent, to **PAP** reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex vivo can induce antigen-specific cellular immunity in **prostate cancer** patients, warranting further studies of this mode of immunotherapy.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:444894 CAPLUS

DN 134:84982

TI PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome

AU Ponniah, Sathibalan; Arah, Ifeyinwa; Alexander, Richard B.

CS Division of Urology, University of Maryland School of Medicine, Baltimore, MD, USA

SO Prostate (New York) (2000), 44(1), 49-54
CODEN: PRSTDS; ISSN: 0270-4137

PB Wiley-Liss, Inc.

DT Journal

LA English

AB BACKGROUND. Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the **prostate** could be candidate antigens in auto-immune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. METHODS. Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by d. gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with

IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (**GM-CSF**). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. RESULTS. In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (**PAP**) or β-microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. CONCLUSIONS. The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic **cancer**.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 11:57:08 ON 21 JUN 2006)

FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT 11:57:29 ON 21 JUN 2006

L1 31 S (PAP AND (GM (W) CSF) AND CANCER)
L2 25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L3 17 S (L2 AND PROSTATE)
L4 17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d l2 bib abs 1-25

L2 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2005:1321617 CAPLUS
TI Safety and immunological efficacy of a prostate **cancer** plasmid DNA vaccine encoding prostatic acid phosphatase (**PAP**)
AU Johnson, Laura E.; Frye, Thomas P.; Arnot, Alana R.; Marquette, Carrie; Couture, Larry A.; Gendron-Fitzpatrick, Annette; McNeel, Douglas G.
CS Department of Medicine, Section of Medical Oncology, K4/518 Clinical Science Center, University of Wisconsin-Madison, Madison, WI, 53792, USA
SO Vaccine (2006), 24(3), 293-303
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier B.V.
DT Journal
LA English
AB Prostatic acid phosphatase (**PAP**) is a prostate tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clin. benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat **PAP** can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunol. efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human **PAP**, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-wk intervals with 100, 500, or 1500 μg pTVG-HP with 5 μg recombinant rat **GM-CSF** protein given as a vaccine adjuvant. An addnl. 12 male Lewis rats served as controls with groups immunized with 1500 μg of a parental DNA vector not encoding human **PAP**, and a group that received **GM-CSF** protein only without plasmid DNA. Groups of animals (n = 3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunol. anal. No significant toxicities were observed in terms of animal wts., histopathol., hematol. changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically

different from control animals. The vaccine was found to be effective in eliciting **PAP**-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and nos. of immunizations. **PAP**-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting **PAP**-specific cellular and humoral immune responses. These findings support the further clin. evaluation of pTVG-HP in patients with prostate **cancer**.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:72938 CAPLUS
TI Provenge: prostate **cancer** therapy
AU McIntyre, J. A.; Fernandez, D.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2005), 30(9), 892-895
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. There are few therapeutic options available for the treatment of hormone-refractory prostate **cancer** (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing prostate-specific T-cell-mediated immunity. Provenge (APC-8015) is an immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (**PAP**), an antigen found in 95% of prostate **cancers**, and granulocyte-macrophage colony-stimulating factor (**GM-CSF**). Early clin. studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge, with increases in prostate-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1127402 CAPLUS
DN 142:54751
TI Alternative reading frame peptides as antigens for the prophylaxis and treatment of **cancer** and infectious diseases
IN Graddis, Thomas; Laus, Reiner; Diegel, Michael; Vidovic, Damis
PA Dendreon Corporation, USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004111075 | A2 | 20041223 | WO 2004-US6979 | 20040305 |
| | WO 2004111075 | C1 | 20050519 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| | CA 2514288 | AA | 20041223 | CA 2004-2514288 | 20040305 |
| | US 2005112134 | A1 | 20050526 | US 2004-794514 | 20040305 |
| | EP 1601684 | A2 | 20051207 | EP 2004-749357 | 20040305 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| PRAI | US 2003-453131P | P | 20030305 | | |
| | WO 2004-US6979 | W | 20040305 | | |

AB Alternative reading frame (ARF) peptides associated with disease conditions and that can be recognized by antigen presenting cells (APC) and dendritic cells (DC) are described for use as antigens in the diagnosis, treatment, and prevention of diseases including **cancer** and infectious diseases. These peptides may arise from frameshifting, use of alternative start codons, ribosomal skipping, suppression of termination of translation, translation of antisense transcripts, splice variants or use of cryptic promoters. Alternative reading frame peptides derived from the HER-2 receptor gene were incubated with mouse dendritic cells in vitro and the cells reintroduced into the donor mice. Mice challenged with B16 cells blocked tumor growth, whereas animals treated with inframe HER-2 proteins did not.

L2 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:333598 CAPLUS
DN 140:373894
TI CEA-specific monoclonal antibodies or fragments with therapeutic agents for treating CEA-expressing **cancers** and diseases
IN Goldenberg, David M.; Hansen, Hans J.
PA Immunomedics, Inc., USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004032962 | A1 | 20040422 | WO 2002-US32307 | 20021011 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2501757 | AA | 20040422 | CA 2002-2501757 | 20021011 |
| | AU 2002332087 | A1 | 20040504 | AU 2002-332087 | 20021011 |
| | EP 1558284 | A1 | 20050803 | EP 2002-769028 | 20021011 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | JP 2006507263 | T2 | 20060302 | JP 2004-542990 | 20021011 |
| | CA 2501616 | AA | 20040422 | CA 2003-2501616 | 20031008 |
| | WO 2004032857 | A2 | 20040422 | WO 2003-US31801 | 20031008 |
| | WO 2004032857 | C1 | 20050407 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| AU 2003282752 | A1 | 20040504 | AU 2003-282752 | 20031008 |
| US 2004191248 | A1 | 20040930 | US 2003-680734 | 20031008 |
| EP 1572131 | A2 | 20050914 | EP 2003-774636 | 20031008 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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|---|---|---|---|
| PRAI US 2002-416531P | P | 20021008 | |
| WO 2002-US32307 | W | 20021011 | |
| US 2003-467161P | P | 20030502 | |
| WO 2003-US31801 | W | 20031008 | |

AB The present invention provides a composition comprising naked humanized, chimeric and human Class III anti-CEA monoclonal antibody and a therapeutic agent, which is useful for treatment of CEA-expressing **cancers** and other diseases, and methods of treatment using this composition The anti-CEA monoclonal antibody or fragment is a humanized or chimeric MN-14 antibody or fragment or fully human MN-14 antibody or fragment.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:331925 CAPLUS
DN 140:355848
TI humanized or chimeric derivatives of murine monoclonal anti-CEA antibody MN-14 and conjugates for **cancer** therapy
IN Goldenberg, David M.; Hansen, Hans J.
PA Immunomedics, Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2004032857 | A2 | 20040422 | WO 2003-US31801 | 20031008 |
| WO 2004032857 | C1 | 20050407 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| WO 2004032962 | A1 | 20040422 | WO 2002-US32307 | 20021011 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| CA 2501616 | AA | 20040422 | CA 2003-2501616 | 20031008 |
| AU 2003282752 | A1 | 20040504 | AU 2003-282752 | 20031008 |
| EP 1572131 | A2 | 20050914 | EP 2003-774636 | 20031008 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI US 2002-416531P P 20021008
WO 2002-US32307 A 20021011
US 2003-467161P P 20030502
WO 2003-US31801 W 20031008

AB The present invention provides a composition comprising naked humanized or chimeric murine monoclonal antibody MN-14 and a therapeutic agent, which is useful for treatment of CEA expressing **cancers** and other diseases, and methods of use in treatment using this composition

L2 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:287861 CAPLUS
DN 140:320038
TI Chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation
IN Goldenberg, David M.; Hansen, Hans; Leung, Shui-on
PA Immunomedics, Inc., USA; Mccall, John Douglas
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004029093 | A2 | 20040408 | WO 2003-GB4229 | 20030930 |
| | WO 2004029093 | A3 | 20040603 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CN 1542019 | A | 20041103 | CN 2003-123054 | 20030429 |
| | CA 2500250 | AA | 20040408 | CA 2003-2500250 | 20030930 |
| | AU 2003269225 | A1 | 20040419 | AU 2003-269225 | 20030930 |
| | EP 1546204 | A2 | 20050629 | EP 2003-751001 | 20030930 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRAI US 2002-414341P P 20020930
WO 2003-GB4229 W 20030930

AB The present invention provides humanized, chimeric and human MN3 antibodies, fusion proteins, and fragments that bind NCA90 and NCA95 antigens. The antibodies, fusion proteins, and fragments thereof, as well as combinations with other suitable antibodies, are useful for the treatment and diagnosis of granulocyte related disorders and diseases, such as leukemia.

L2 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:270002 CAPLUS
DN 140:302326
TI Immunotherapeutic compositions comprising antigen presenting cells (APCs) stimulated by fusion proteins (such as APC binding protein fused to tumor-associated antigen), and use of compositions in treatment of moderately to well-differentiated **cancers**
IN Laus, Reiner; Gold, Mitchell; Madhusudan, Peshwa; Pickering, Grant; Kylstra, Jelle; Peshwa, Madhusudan
PA Dendreon Corporation, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004026238 | A2 | 20040401 | WO 2003-US29176 | 20030919 |
| | WO 2004026238 | C1 | 20040722 | | |
| | WO 2004026238 | A3 | 20041209 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2497554 | AA | 20040401 | CA 2003-2497554 | 20030919 |
| | AU 2003267254 | A1 | 20040408 | AU 2003-267254 | 20030919 |
| | US 2004161413 | A1 | 20040819 | US 2003-666122 | 20030919 |
| | EP 1540627 | A2 | 20050615 | EP 2003-749725 | 20030919 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRAI | US 2002-412271P | P | 20020920 | | |
| | US 2003-475355P | P | 20030602 | | |
| | US 2003-475335P | P | 20030602 | | |
| | WO 2003-US29176 | W | 20030919 | | |

AB The invention discloses immunotherapeutic compns. comprising activated antigen presenting cells (APCs), wherein said APCs were obtained from **cancer** patients and stimulated by exposure ex vivo to a fusion protein composed of a APC binding protein and tumor-associated (specific) antigen. The invention also discloses the use of said stimulated/activated APCs in treatment of patients with moderately to well-differentiated **cancer** cells. The invention further provides a method of assessing in **cancer** patients the susceptibility of **cancer** to said immunotherapeutic compns. As way of illustration, the invention discloses a fusion protein (APC8015) composed of a portion of prostate tumor-associated protein human prostatic acid phosphatase (huPAP) at the N-terminus and a portion of APC/DC binding protein human granulocyte-macrophage colony stimulating factor (huGM-CSF) at the C-terminus. APC stimulated by exposure ex vivo to said **PAP /GM-CSF** fusion protein were effective in activating T cells to produce a cytotoxic cellular response against huPAP. Finally, the invention discloses the amino acid sequences of huPAP and huGM-CSF. In the examples, the invention demonstrated that the therapeutic efficacy of immunotherapeutic compns. comprising APCs stimulated with **PAP /GM-CSF** fusion protein correlates with the differentiation state of the prostate **cancer** cells. Specifically, it was demonstrated that patients exhibiting moderately to well-differentiated prostrate **cancer** cells were susceptible to treatment with said immunotherapeutic composition The invention also demonstrated the efficacy of a combined immunotherapeutic treatment regimen that includes administration of **PAP/GM-CSF**-pulsed dendritic cells in conjunction with administration of humanized anti-VEGF monoclonal antibody Bevacizumab in patients having a serol. progression of prostate **cancer**.

L2 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:120888 CAPLUS
DN 140:198085
TI Chimeric and humanized anti-α-fetoprotein antibodies Immu31 and fragments for diagnosis and therapy of hepatocellular carcinoma, hepatoblastoma and germ cell tumors

IN Hansen, Hans; Qu, Zhengxing; Goldenberg, David M.
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004013180 | A2 | 20040212 | WO 2003-GB3325 | 20030801 |
| | WO 2004013180 | A3 | 20040916 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2494310 | AA | 20040212 | CA 2003-2494310 | 20030801 |
| | AU 2003248982 | A1 | 20040223 | AU 2003-248982 | 20030801 |
| | US 2004235065 | A1 | 20041125 | US 2003-631722 | 20030801 |
| | EP 1546203 | A2 | 20050629 | EP 2003-766456 | 20030801 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRAI | US 2002-399707P | P | 20020801 | | |
| | WO 2003-GB3325 | W | 20030801 | | |

AB The present invention provides humanized, chimeric and human anti-alpha-fetoprotein antibodies, fusion proteins, and fragments thereof. The antibodies, fusion proteins, and fragments thereof, as well as combinations with other suitable antibodies, are useful for the treatment and diagnosis of hepatocellular carcinoma, hepatoblastoma, germ cell tumors, carcinoma and other AFP-producing tumors.

L2 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:589231 CAPLUS
DN 141:134058
TI Methods and compositions for treating prostate **cancer** using DNA vaccines
IN McNeel, Douglas
PA Wisconsin Alumni Research Foundation, USA
SO U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004142890 | A1 | 20040722 | US 2003-669474 | 20030925 |
| PRAI | US 2002-413777P | P | 20020927 | | |

AB A DNA vaccine for the treatment of prostate **cancer**, comprising a plasmid vector comprising a nucleotide sequence encoding prostatic acid phosphatase (**PAP**) operably linked to a transcription regulatory element, wherein upon administration to a mammal a cytotoxic immune reaction against cells expressing **PAP** is induced. In preferred embodiment, the **PAP** encoded is a xenoantigen highly homologous to the autoantigen **PAP** of the mammal. Also disclosed are methods for inducing prostatitis, or inducing immune reaction to **PAP**, or treating prostate **cancer** in a mammal, using the DNA vaccine and pharmaceutical compns. comprising the vaccine. Preferably, xenoantigen vaccination is followed by boosting with autoantigen **PAP** from the same animal species as the mammal being

treated. Lewis rats immunized with pTVG-HP, encoding human **PAP**, developed **PAP**-specific cellular immunity and prostate tissue inflammation.

L2 ANSWER 10 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-21964 BIOTECHDS
TI Treating **cancer** with an immunotherapeutic composition comprises determining differentiation state of **cancer** cells, where presence of moderately to well-differentiated cells indicates patient susceptible to treatment with the composition;
composition for **cancer** immunotherapy comprises dendrite cell exposed to tumor-associated antigen
AU LAUS R; GOLD M H; PESHWA M; PICKERING G; KYLSTRA J
PA DENDREON CORP
PI US 2004161413 19 Aug 2004
AI US 2003-666122 19 Sep 2003
PRAI US 2003-666122 19 Sep 2003; US 2002-412271 20 Sep 2002
DT Patent
LA English
OS WPI: 2004-614827 [59]
AN 2004-21964 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Treating (M1) a **cancer** patient with an immunotherapeutic composition where the patient has a **cancer** with moderately to well-differentiated **cancer** cells, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment with an immunotherapeutic composition, and administering the composition, where a reduction of 10% indicates an effective treatment of the **cancer** , is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an immunotherapeutic composition (I) comprising activated, isolated antigen presenting cells (APCs) that are obtained from a patient diagnosed with a **cancer** having a moderate to well-differentiated **cancer** grade and are stimulated by exposure ex vivo to a tumor-associated antigen (TAA); (2) inhibiting (M2) growth of a **cancer** cell in a patient having a moderate to well differentiated **cancer** grade, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment, isolating APCs from the patient, stimulating the APCs by exposure ex vivo to the immunotherapeutic composition comprising a protein conjugate having an N-terminal moiety and a C-terminal moiety, where the APCs are effective to activate T-cells to produce a cytotoxic cellular response against either the N-terminal moiety or the C-terminal moiety and where the level of the T-cell activation is higher than that produced by the APCs when exposed exclusively to the N- or C-terminal moiety, and administering to the patient the stimulated APCs, where a reduction of 10% indicates an effective treatment of the **cancer** and (3) a method of assessing in a **cancer** patient the susceptibility of the **cancer** to an immunotherapeutic composition, comprising isolating from the patient a sample containing the **cancer** cell, and determining the differentiation state of the **cancer** cell, where a moderate to well differentiated **cancer** grade indicates that the **cancer** is susceptible to treatment with an immunotherapeutic composition.

WIDER DISCLOSURE - Also disclosed are nucleic acids, polypeptides, host cells, vectors and antibodies used in the methods of the invention.

BIOTECHNOLOGY - Preferred Method: The composition is (I). Preferred Composition: The TAA of the immunotherapeutic composition is a tumor-specific antigen, or is a component of a protein conjugate comprising an N- and C-terminal moiety. The APCs are dendritic cells. The

**cancer** is soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or prostate. The **cancer** grade corresponds to a Gleason score of at most 7. The patient is not refractory to hormone ablation therapy. The N- or C-terminal moiety is an APC binding protein an/or a TAA. The fusion protein further comprises, between the N- and the C-terminal moiety, a linker peptide. The N- or C-terminal comprises a sequence having at least 70, 80, 90 or 100% identical to huPAP or huGM-CSF with a fully defined sequence of 386 or 144 amino acids (SEQ ID NO: 1 and 3), respectively, as given in the specification.

ACTIVITY - Cytostatic; Immunostimulant. Prior to initiating an immunotherapeutic treatment regimen with **PAP/GM-CSF** fusion protein (APC8015) or placebo, patients were assessed for baseline disease characteristics. To determine the differentiation state of prostate **cancer** cells, prostate tissue samples were isolated from each patient and subjected to analysis by the Gleason scoring methodology as described in Gleason, Urologic Pathology: The Prostate, pp. 171-197 (Tappenhaum, ed., Lee and Fehiger, Philadelphia, Pa., 1977). Time to objective disease progression was defined as progression on bone scan or x-ray or clinical deterioration and the data were subjected to statistical analysis by the Kaplan-Meier methodology. PSA was not used to determine disease progression. The median time to disease progression for the patient population treated with APC8015 was 11.0 weeks whereas the median time to disease progression for the patient population treated with placebo was 9.1 weeks. The data demonstrated that patients having poorly differentiated prostate **cancer** cells were refractory to treatment with APC8015 as evidenced by the absence of a statistically significant difference (p-value=0.431) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo. In contrast, the results obtained for patients exhibiting moderately to well-differentiated prostate **cancer** cells (having a Gleason score of less than or equal to 7) show that such patients were susceptible to treatment with an immunotherapeutic composition as evidenced by the high degree of statistical significance (p-value=0.002) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo.

MECHANISM OF ACTION - None given.

USE - For treating **cancers** including soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or prostate (claimed).

ADMINISTRATION - Routes of administration of the pharmaceutical compositions include oral, pulmonary, intramuscular, intraperitoneal, intravenous, subcutaneous, inhalation, transdermal, nasal, vaginal, rectal and sublingual. No dosages given.

ADVANTAGE - The method is based upon the observation that the grade of a **cancer** cell, being a measure of the cell's differentiation state, is predictive of clinical outcome in **cancer** patients undergoing an immunotherapeutic treatment regimen. Whereas poorly differentiated cells were found to be refractory to an immunotherapeutic treatment regimen, moderately to well-differentiated cells were highly susceptible to treatment with immunotherapeutic compositions. (34 pages)

L2 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:715711 CAPLUS
DN 141:294358
TI Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate **cancer**: a phase 2 trial
AU Burch, Patrick A.; Croghan, Gary A.; Gastineau, Dennis A.; Jones, Lori A.; Kaur, Judith S.; Kylstra, Jelle W.; Richardson, Ronald L.; Valone, Frank

H.; Vuk-Pavlovic, Stanimir
CS Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, MN, USA
SO Prostate (New York, NY, United States) (2004), 60(3), 197-204
CODEN: PRSTDS; ISSN: 0270-4137
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Prostate **cancer** is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (**PAP**) and **GM-CSF**. We enrolled 21 patients with histol. documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomog. scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-pos. PA2024-loaded APCs with admixts. of monocytes, macrophages, B and T cells. APC8015 was infused i.v. twice, 2 wk apart. Two weeks after the second infusion, patients received three s.c. injections of 1.0 mg of PA2024 1 mo apart. We monitored patients' phys. condition, immune response, and laboratory parameters. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/mL at baseline to undetectable levels by week 24 and has remained so for more than 4 yr. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 wk proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 wk. This study demonstrates a definite clin. response of androgen-independent prostate **cancer** to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2003:719518 CAPLUS
DN 139:259962
TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and conjugates for diagnosis and treatment of **cancer**
IN Govindan, Serengulam; Qu, Zhengxing; Hansen, Hans J.; Goldenberg, David M.
PA Immunomedics, Inc., USA; Mccall, John Douglas
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003074566 | A2 | 20030912 | WO 2003-GB885 | 20030303 |
| WO 2003074566 | A3 | 20040304 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| | CA 2478047 | AA | 20030912 | CA 2003-2478047 | 20030303 |
| | AU 2003209447 | A1 | 20030916 | AU 2003-209447 | 20030303 |
| | US 2004001825 | A1 | 20040101 | US 2003-377121 | 20030303 |
| | EP 1483295 | A2 | 20041208 | EP 2003-743420 | 20030303 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | CN 1649903 | A | 20050803 | CN 2003-809918 | 20030303 |
| | JP 2006502698 | T2 | 20060126 | JP 2003-573031 | 20030303 |
| PRAI | US 2002-360229P | P | 20020301 | | |
| | WO 2003-GB885 | W | 20030303 | | |

AB This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in a host. More specifically, the present invention relates to the tumor-associated antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

L2 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:1007015 CAPLUS
DN 140:58438
TI Monoclonal anti-MUC1 antibody PAM4 and chimeric antibodies for diagnosis and therapy of pancreatic **cancer**
IN Gold, David V.; Goldenberg, David M.; Hansen, Hans
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003106497 | A1 | 20031224 | WO 2003-GB2585 | 20030616 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2489469 | AA | 20031224 | CA 2003-2489469 | 20030616 |
| | AU 2003250367 | A1 | 20031231 | AU 2003-250367 | 20030616 |
| | US 2004057902 | A1 | 20040325 | US 2003-461878 | 20030616 |
| | EP 1521775 | A1 | 20050413 | EP 2003-760086 | 20030616 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | JP 2006507803 | T2 | 20060309 | JP 2004-513328 | 20030616 |
| PRAI | US 2002-388313P | P | 20020614 | | |
| | WO 2003-GB2585 | W | 20030616 | | |

AB This invention relates to monovalent and multivalent, monospecific antibodies and to monovalent and multivalent, multispecific antibodies. One embodiment of these antibodies has one or more identical binding sites

where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these antibodies has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional antibodies in a host. More specifically, the present invention relates to the tumor-associated antibody designated PAM4. The invention further relates to chimeric PAM4 antibodies, and the use of such antibodies in diagnosis and therapy.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:1007014 CAPLUS
DN 140:58437
TI Multivalent humanized monoclonal anti-MUC1 antibody PAM4 for diagnosis and treatment of **cancer**
IN Goldenberg, David M.; Hansen, Hans; Qu, Zhengxing
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003106495 | A2 | 20031224 | WO 2003-GB2593 | 20030616 |
| | WO 2003106495 | A3 | 20040401 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2489467 | AA | 20031224 | CA 2003-2489467 | 20030616 |
| | AU 2003277087 | A1 | 20031231 | AU 2003-277087 | 20030616 |
| | US 2005014207 | A1 | 20050120 | US 2003-461885 | 20030616 |
| | EP 1519958 | A2 | 20050406 | EP 2003-740743 | 20030616 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003011799 | A | 20050510 | BR 2003-11799 | 20030616 |
| | CN 1675245 | A | 20050928 | CN 2003-819294 | 20030616 |
| | JP 2006513695 | T2 | 20060427 | JP 2004-513326 | 20030616 |
| PRAI | US 2002-388314P | P | 20020614 | | |
| | WO 2003-GB2593 | W | 20030616 | | |

AB This invention relates to monovalent and multivalent, monospecific antibodies and to multivalent, multispecific antibodies. One embodiment of these antibodies has one or more identical binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these antibodies has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional antibodies in a host. More specifically, the present invention relates to the tumor-associated antibody designated PAM4. The invention further relates to humanized and human PAM4 antibodies, and the use of such antibodies in diagnosis and therapy.

L2 ANSWER 15 OF 25 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2003:37239077 BIOTECHNO
TI Cell therapy and prostate **cancer**
THERAPIE CELLULAIRE ET **CANCER** DE LA PROSTATE
AU Eymard J.-C.; Bernard J.
CS J.-C. Eymard, U. Fonct. Rech. Clin./Therapie Cell., Institut Jean-Godinot, 1, av. du gen. Koenig, 51056 Reims Cedex, France. E-mail: jc.eymard@reims.fnclcc.fr
SO Bulletin du Cancer, (2003), 90/8-9 (734-743), 63 reference(s)
CODEN: BUCABS ISSN: 0007-4551
DT Journal; General Review
CY France
LA French
SL English; French
AB Hormonotherapy is the standard treatment for advanced prostate **cancer** but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of **cancer** cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use **GM-CSF** gene-transduced allogenic cells.
The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two prostate antigens have already been used, PSMA evaluated in 130 patients and a fusion protein **PAP-GM-CSF** (Provenge®) in 144 patients.
All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to amplify vaccine response and clinical efficacy.

L2 ANSWER 16 OF 25 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2005226190 ESBIOBASE
TI Session II: Tumor antigens - Prostate **cancer** antigens and vaccines
AU Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.; Belldegrun A.; Logothetis C.; Papandreou C.
CS Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA, United States.
SO Cancer Immunology, Immunotherapy, (2003), 52/SUPPL. 1 (S8-S9+S27)
CODEN: CIIMDN ISSN: 0340-7004
DT Journal; Conference Article
CY Germany, Federal Republic of
LA English
SL English
AB The clinical development of prostate **cancer** vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those **cancers** for which tumor and immune cells are readily available.
Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory prostate **cancer** (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During

the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate **cancer**: prostate-specific membrane antigen (PSMA), prostate-specific antigen (PSA), and prostatic acid phosphatase ( **PAP**). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and **PAP** as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (**GM-CSF**, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. 

L2 ANSWER 17 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-15068 BIOTECHDS
TI Eliciting or enhancing immune response to human self tumor antigen e.g. HER-2/neu protein for preventing tumor occurrence by immunizing individual with foreign protein or its portion homologous to the self antigen;
recombinant vaccine against **cancer**
AU CHEEVER M A; DISIS M L
PA CHEEVER M A; DISIS M L
PI US 2002019331 14 Feb 2002
AI US 1996-88951 1 Apr 1996
PRAI US 1998-88951 2 Jun 1998
DT Patent
LA English
OS WPI: 2002-303155 [34]
AN 2002-15068 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Eliciting or enhancing an immune response to a human self tumor antigen involves immunizing a human being with a foreign protein homologous to the antigen or with a foreign peptide homologous to a portion of the antigen.
BIOTECHNOLOGY - Preferred Method: The foreign protein or peptide is present in a carrier or diluent. The method additionally involves the use of an adjuvant.
ACTIVITY - Antitumor.
MECHANISM OF ACTION - Immune response enhancer or elicitor (claimed). Rats (Fischer strain 344 (CDF (F-344)/CrIBR)) were immunized with recombinant human HER-2/neu intracellular domain protein (hICD) (50

microg) or immunoaffinity column purified rat neu protein (50 microg). Proteins were administered with either complete Fruend's antigen (CFA) or murine granulocyte macrophage-colony stimulating factor (**GM-CSF**) 5 microg as adjuvants. Control groups received adjuvant alone. Animals underwent immunizations each 14-16 days apart. 18-10 days after the second immunizations animals were assessed for immunologic response. Rats immunized with hICD developed high titer human and rat neu specific antibodies. All rats immunized with hICD developed significant antibody responses specific for human HER-2/neu protein, with titers greater than 1:200,000. Human HER-2/neu ICD is 92% homologous to rat neu ICD at the amino acid level. Analysis was performed to discern whether the human HER-2/neu specific antibodies were cross-reactive with rat neu. Rats immunized with hICD with either **GM-CSF** or CFA as an adjuvant had high titer antibody responses specific for rat neu. The magnitude of the rat neu specific antibody responses was nearly identical to that of the human HER-2/neu specific response. Delayed type hypersensitivity (DTH) responses were used to initially evaluate for the presence of the T cell responses to neu in rats immunized with HER-2/neu. HER-2/neu specific DTH responses were detected in animals who received hICD in **GM-CSF** or CFA. The responses were cross-reactive to rat neu protein. DTH was not detected in animals immunized with rat neu protein or with adjuvants alone. Immunization of rats with hICD elicits detectable T cell responses specific for both human and rat neu protein. T cell proliferative responses were evaluated in rats immunized with hICD plus either **GM-CSF** or CFA. T cell responses to hICD protein were detected from lymph nodes draining the inoculation site. T cell responses to rat neu protein were also detected, although at a lower magnitude than the hICD response.

USE - For eliciting or enhancing an immune response to a human self tumor antigen which a protein expression product of an over expressed human oncogene such as HER-2/neu protein, or a portion of the human HER-2/neu protein, where the portion includes the intracellular domain of the human HER-2/neu protein. Optionally the immune response is elicited or enhanced against an antigen or antigen portion which is an organ-specific or tissue-specific differentiation antigen associated with tumor cells, or a portion of the antigen. Preferably the organ- or tissue-specific differentiation antigen is an antigen associated with prostate **cancer**, e.g. prostatic acid phosphatase (**PAP**) or prostate specific antigen (PSA) (all claimed). The method is useful for eliciting or enhancing an immune response as a preventing measure to prevent tumor occurrence or recurrence, or as therapy to arrest tumor growth or eradicate existence tumors or to prolong the survival.

ADMINISTRATION - The vaccine composition is administered by intradermal, subcutaneous or intravenous routes. Dosages range from 1 microg/kg-1 mg/kg, preferably 5-200 microg/kg.

ADVANTAGE - The method overcomes immunological tolerance which exists and represents a potential barrier to effectively vaccinating against human self tumor antigens, by immunizing an individual with a protein or peptide that is foreign (i.e., not identical to that in the individual) but nevertheless homologous to an individuals self tumor antigen or its portion. (26 pages)

L2 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:417000 CAPLUS
DN 135:32745
TI Antigen-binding fragments specific for tumor associated antigens
IN Dan, Michael; Entwistle, Joycelyn; Fast, Darren; Kaplan, Howard; Lewis, Keith; MacDonald, Glen; Maiti, Pradip
PA Novopharm Biotech Inc., Can.
SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001040292 | A1 | 20010607 | WO 1999-CA1141 | 19991129 |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | WO 1999-CA1141 | | 19991129 | | |

AB The present invention relates to antigen-binding fragments that are specific for stress protein-peptide complexes specifically associated with tumors, particularly human tumors, and compns. thereof. The compns. are suitable for diagnostic and pharmaceutical use. The invention further provides methods of making and screening for the antigen-binding fragments. The invention further encompasses compns. containing **cancer**-associated stress protein-peptide complexes (including derivs. thereof) and methods of use thereof. The **cancer**-specific stress protein-peptide complexes (SPPC's) are particularly useful in eliciting **cancer**-specific immunogenic responses against a plurality of **cancers**. The invention also provides novel phage display libraries for use in producing further SPPCs and anti-SPPCs of the invention.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:224352 CAPLUS
DN 134:251211
TI Monoclonal antibody to C-antigen: Prophylaxis and detection of **cancer**
IN Dan, Michael D.; Maiti, Pradip K.; Kaplan, Howard A.
PA Viventia Biotech, Inc., Can.
SO U.S., 56 pp., Cont.-in-part of U.S. Ser. No. 657,449, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6207153 | B1 | 20010327 | US 1997-862124 | 19970522 |
| | CA 2255540 | AA | 19971127 | CA 1997-2255540 | 19970522 |
| | CN 1229436 | A | 19990922 | CN 1997-194815 | 19970522 |
| | NZ 505305 | A | 20020628 | NZ 1997-505305 | 19970522 |
| | KR 2000015893 | A | 20000315 | KR 1998-709444 | 19981121 |
| | AU 775448 | B2 | 20040729 | AU 2000-72432 | 20001220 |
| | US 2003021779 | A1 | 20030130 | US 2001-782397 | 20010213 |
| | US 2004091484 | A1 | 20040513 | US 2003-651453 | 20030829 |
| PRAI | US 1996-657449 | B2 | 19960522 | | |
| | AU 1997-33696 | A3 | 19970522 | | |
| | NZ 1997-332566 | A1 | 19970522 | | |
| | US 1997-862124 | A1 | 19970522 | | |
| | US 2001-782397 | B1 | 20010213 | | |

AB The authors disclose preparation and sequence characterization of monoclonal antibody H11 that specifically binds to an antigen (termed "C-antigen") expressed by diverse tumors and tumor cell lines. The C-antigen was not found on normal cells. Also disclosed are polynucleotides and single chain antibodies based on H11 for application in therapy and tumor imaging.

RE.CNT 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:869162 CAPLUS
DN 142:233296
TI Consensus peptide presenting entities, screening methods, and use for the treatment and diagnosis of tumors.
IN Maiti, Pradip K.; Herman, William; Dan, Michael D.; Kaplan, Howard A.; MacDonald, Glen C.; Entwistle, Jocelyn M.; Lewis, Keith E.; Fast, Darren G.
PA Novopharm Biotech Inc., Can.
SO Can. Pat. Appl., 155 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI CA 2290722 | AA | 20010608 | CA 1999-2290722 | 19991208 |
| PRAI CA 1999-2290722 | | 19991208 | | |

AB The invention provides antigen-binding-fragments specific for tumor cells and effective in treatment and/or diagnosing tumors. Methods of use are also provided as are methods for screening for addnl. such antigen-binding-fragments and the products obtained thereby.

L2 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 2000:445203 CAPLUS
DN 133:87934
TI Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for prostate **cancer**
AU Burch, Patrick A.; Breen, Jami K.; Buckner, Jan C.; Gastineau, Dennis A.; Kaur, Judith A.; Laus, Reiner L.; Padley, Douglas J.; Peshwa, Madhusudan V.; Pitot, Henry C.; Richardson, Ronald L.; Smits, Bouwien J.; Sopapan, Pitsata; Strang, George; Valone, Frank H.; Vuk-Pavlovic, Stanimir
CS Divisions of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905, USA
SO Clinical Cancer Research (2000), 6(6), 2175-2182
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB We attempted to induce therapeutic immunity against prostate-derived tissues in patients suffering from progressive hormone-refractory metastatic prostate carcinoma. Thirteen patients were treated with two infusions, 1 mo apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (**GM-CSF**) and human prostatic acid phosphatase (**PAP**). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating prostate-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by **GM-CSF** ($P = 0.0004$) and **PAP** ($P = 0.0001$), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against **PAP** and **GM-CSF**. However, antibodies to **GM-CSF** and, to a much lesser extent, to **PAP** reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex

vivo can induce antigen-specific cellular immunity in prostate **cancer** patients, warranting further studies of this mode of immunotherapy.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:444894 CAPLUS
DN 134:84982
TI PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome
AU Ponniah, Sathibalan; Arah, Ifeyinwa; Alexander, Richard B.
CS Division of Urology, University of Maryland School of Medicine, Baltimore, MD, USA
SO Prostate (New York) (2000), 44(1), 49-54
CODEN: PRSTDS; ISSN: 0270-4137
PB Wiley-Liss, Inc.
DT Journal
LA English
AB BACKGROUND. Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the prostate could be candidate antigens in auto-immune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. METHODS. Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by d. gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (**GM-CSF**). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. RESULTS. In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (**PAP**) or β-microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. CONCLUSIONS. The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic **cancer**.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:661515 CAPLUS
DN 129:274703
TI Immunotherapy of B-cell malignancies using anti-CD22 antibodies
IN Goldenberg, David M.
PA IMMUNOMEDICS, INC., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9842378 | A1 | 19981001 | WO 1998-US5075 | 19980317 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, | | | | |

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| US 6183744 | B1 | 20010206 | US 1998-38955 | 19980312 |
| CA 2284829 | AA | 19981001 | CA 1998-2284829 | 19980317 |
| AU 9867610 | A1 | 19981020 | AU 1998-67610 | 19980317 |
| AU 728325 | B2 | 20010104 | | |
| EP 969866 | A1 | 20000112 | EP 1998-912936 | 19980317 |
| EP 969866 | B1 | 20050615 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001518930 | T2 | 20011016 | JP 1998-545761 | 19980317 |
| EP 1431311 | A1 | 20040623 | EP 2004-75775 | 19980317 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| EP 1459768 | A2 | 20040922 | EP 2004-75774 | 19980317 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 297759 | E | 20050715 | AT 1998-912936 | 19980317 |
| ES 2241129 | T3 | 20051016 | ES 1998-912936 | 19980317 |
| IN 189313 | A | 20030208 | IN 1998-DE705 | 19980320 |
| ZA 9802438 | A | 19981104 | ZA 1998-2438 | 19980323 |
| PRAI US 1997-41506P | P | 19970324 | | |
| EP 1998-912936 | A3 | 19980317 | | |
| WO 1998-US5075 | W | 19980317 | | |

AB B-Cell malignancies, such as the B-cell subtype of non-Hodgkin's lymphoma and chronic lymphocytic leukemia, are significant contributors to **cancer** mortality. The response of B-cell malignancies to various forms of treatment is mixed. Traditional methods of treating B-cell malignancies, including chemotherapy and radiotherapy, have limited utility due to toxic side effects. Immunotherapy with anti-CD20 antibodies have also provided limited success. The use of antibodies that bind with the CD22 antigen, however, provides an effective means to treat B-cell malignancies such as indolent and aggressive forms of B-cell lymphomas, and acute and chronic forms of lymphatic leukemias. Moreover, immunotherapy with anti-CD22 antibodies requires comparatively low doses of antibody protein, and can be used effectively in multimodal therapies. Immunoconjugates comprising anti-CD22 antibody and radioisotope or cytokine, and combination treatment with chemotherapeutic agent are also disclosed.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 25 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
DUPLICATE
AN 1998:28369021 BIOTECHNO
TI Defective expression of granulocyte-macrophage colony-stimulating factor/interleukin-3/interleukin-5 receptor common β chain in children with acute myeloid leukemia associated with respiratory failure
AU Dirksen U.; Hattenhorst U.; Schneider P.; Schroten H.; Gobel U.; Bocking A.; Muller K.-M.; Murray R.; Burdach S.
CS Dr. U. Dirksen, Pediatric Hematology/Oncology Dept., Children's Hospital Medical Center, 14.82 Moorenstr. 5, D-40225 Duesseldorf, Germany. E-mail: dirksen@uni-duesseldorf.de
SO Blood, (15 AUG 1998), 92/4 (1097-1103), 35 reference(s)
CODEN: BLOOAW ISSN: 0006-4971
DT Journal; Article
CY United States
LA English
SL English
AB Deficiency of the granulocyte-macrophage colony-stimulating factor (

GM- CSF)/interleukin-3 (IL-3)/IL-5 receptors common β chain (βc) is a cause of fatal respiratory failure. βc deficiency manifests as pulmonary alveolar proteinosis (PAP). PAP has heterogenous etiologies that may be genetic or aquired. Some cases of PAP have been reported to be associated with hematologic malignancies such as acute myeloid leukemia (AML). in mice, the PAP phenotype was generated by targeted deletion of the gene for βc and can be treated by transplantation of wild-type bone marrow into βc -/- mice. Thus, our findings in βc -/- mice provide evidence for a causal relationship between the lung disease and the hematopoietic system. We describe here expression defects of βc or βc plus GM-CSF receptor α chain (GM-CSFR α) in 3 pediatric patients with AML and PAP symptoms. All of the patients' leukemic cells failed to express normal levels of βc. The leukemic cells of patients number 2 and 3 additionally lacked the expression of GM-CSFR α, as shown by flow cytometry. Strikingly reduced or absent function of βc was demonstrated in clonogenic progenitor assays with absent colony-forming unit (CFU) growth after GM-CSF or IL-3 stimulation. The response to growth factors acting via a growth factor receptor distinct from the GM-CSF/IL-3/IL-5 system (recombinant human granulocyte colony-stimulating factor ¢rhG-CSF!) was normal. After antileukemic treatment, the pulmonary symptoms resolved and βc or βc plus GM-CSFR α expression was normal. Our findings provide evidence that a defect in the expression of βc or βc plus GM-CSFR α on AML blasts can be associated with respiratory failure in patients with AML.

L2 ANSWER 25 OF 25 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 1997107060 ESBIOBASE
TI Effects of Phytolacca acinosa polysaccharides I with different schedules on its antitumor efficiency in tumor bearing mice and production of IL-1, IL-2, IL-6, TNF, CSF activity in normal mice
AU Wang H.-B.; Zheng Q.-W.
CS H.-B. Wang, Department of Pharmacology, College of Pharmacy, Second Military Medical University, Shanghai 200433, China.
SO Immunopharmacology and Immunotoxicology, (1997), 19/2 (197-213), 29 reference(s)
CODEN: IITOEF ISSN: 0892-3973
DT Journal; Article
CY United States
LA English
SL English
AB Effects of Phytolacca acinosa polysaccharides I (PAP-I), 5-40 mg/kg in timing of 7 times/wk, 3 times/wk and 1 time/wk on their antitumor efficiency in Sarcoma-180 bearing mice were comparatively investigated. The results confirmed that PAP-I (10 mg/kg, 3 times/wk) reached its optimal antitumor efficiency. Concanavalin A-, lipopolysaccharides-induced lymphocyte proliferation and the IL-2 production were tested in normal mice which were treated with PAP -I, 5-50 mg/kg in timing of 1 time/wk and 3 times/wk. The results showed that PAP-I could augment lymphocyte proliferation and IL-2 production in the group treated with PAP-I in timing of once a week. However, in the group 3 times/wk, PAP-I could significantly weaken lymphocyte proliferation and IL-2 production. Further studies on IL-1, TNF and IL-6 secreted from macrophages and the level of CSF activity in serum of normal mice with different schedules showed that PAP-I (10 mg/kg, 3 times/wk) was the best one in regulating the production of IL-1, TNF, IL-6 and CSF activity. M-CSF was confirmed in the serum by using monoclonal antibody of IL-3, GM -CSF and polyclonal antibody of M-CSF. These results suggested that the antitumor effect of PAP-I, may be mainly related to its augmenting effect on macrophages in mice.

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     11:57:29 ON 21 JUN 2006
L1            31 S (PAP AND (GM (W) CSF) AND CANCER)
L2            25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L3            17 S (L2 AND PROSTATE)
L4            17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)
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Last logoff:  19jun06 10:05:08
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***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)

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***File 141, Reader's Guide Abstracts
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***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)
*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.
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***File 196, FINDEX
***File 468, Public Opinion Online (POLL)
Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
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 >>>a specific database by entering HELP NEWS <file number>.<<<
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File   1:ERIC 1966-2006/May
       (c) format only 2006 Dialog

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>>>Unrecognizable Command
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B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34
       21jun06 10:39:42 User290558 Session D54.1
            $1.12    0.321 DialUnits File1
     $1.12  Estimated cost File1
     $0.53  INTERNET
     $1.65  Estimated cost this search
     $1.65  Estimated total session cost   0.321 DialUnits

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  File 155:MEDLINE(R) 1951-2006/Jun 20
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for information about recent updates added to MEDLINE.
  File 159:Cancerlit 1975-2002/Oct
        (c) format only 2002 Dialog
 *File 159: Cancerlit is no longer updating.
Please see HELP NEWS159.
  File  10:AGRICOLA 70-2006/May
        (c) format only 2006 Dialog
  File 203:AGRIS 1974-2006/Mar
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        (c) 2006 ProQuest Info&Learning
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        (c) 2006 The Thomson Corporation
  File 467:ExtraMED(tm) 2000/Dec
        (c) 2001 Informania Ltd.
 *File 467: F467 will close on February 1, 2006.                    7.
  File  73:EMBASE 1974-2006/Jun 21
        (c) 2006 Elsevier Science B.V.
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
        (c) 1998 Inst for Sci Info
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/Jun W3
        (c) 2006 Inst for Sci Info

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S (PSA AND (GM (W) CSF) AND PROSTATE)
           54958  PSA
          137699  GM
          234248  CSF
           60986  GM(W)CSF
          345249  PROSTATE
      S1     137  (PSA AND (GM (W) CSF) AND PROSTATE)
?

RD S1
      S2      65  RD S1  (unique items)
?


Set     Items   Description
S1        137   (PSA AND (GM (W) CSF) AND PROSTATE)
S2         65   RD S1  (unique items)
?

S (PAP AND (GM (W) CSF) AND PROSTATE)
           38783  PAP
          137699  GM
          234248  CSF
           60986  GM(W)CSF
          345249  PROSTATE
      S3      28  (PAP AND (GM (W) CSF) AND PROSTATE)
?

RD S3
      S4      11  RD S3  (unique items)
?
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TYPE S4/FULL/1-11

**4/9/1 (Item 1 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)


20889595 PMID: 16752945
**Sipuleucel-T: APC 8015, APC-8015, Prostate Cancer Vaccine - Dendreon.**
Drugs in R&D (New Zealand) 2006, 7 (3) p197-201, ISSN 1174-5886--Print Journal Code: 100883647
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Data Review
Subfile: INDEX MEDICUS

Sipuleucel-T [APC 8015, Provenge((R))] is an autologous, dendritic cell-based vaccine under development with Dendreon Corporation for the treatment of androgen-independent and androgen-dependent prostate cancer. It was generated using the company's active immunotherapy platform to stimulate a patient's own immune system to specifically target and destroy cancer cells, while leaving healthy cells unharmed. This approach could provide patients with a meaningful survival benefit and an improved tolerability profile over exisiting anticancer therapies. Sipuleucel-T selectively targets the prostate-specific antigen (PSA) known as prostatic acid phosphatase (PAP) that is expressed in approximate, equals95% of prostate cancers. It is produced by ex vivo exposure of dendritic cell precursors to PA 2024, a recombinant fusion protein composed of the PAP target fused to granulocyte-macrophage colony-stimulating factor (GM-CSF) and incorporated into Dendreon's proprietary Antigen Delivery Cassettetrade mark. Patients are typically administered three intravenous (IV)-infusions of the vaccine over a 1-month period as a complete course of therapy. It is undergoing late-stage clinical evaluation among patients with early and advanced prostate cancer.In November 2003, Kirin Brewery returned to Dendreon the full rights to Sipuleucel-T for Asia. In exchange, Dendreon licensed patent rights relating to the use of certain HLA-DR antibodies to Kirin for $US20 million. This amended agreement enables Dendreon to complete ongoing discussions for a worldwide marketing and sales partnership for Sipuleucel-T. Similarly, Kirin is able to develop its HLA-DR monoclonal antibodies free of potential infringement claims arising from Dendreon's patent rights to HLA-DR. The licensing agreement relates to patent rights owned by Dendreon relating to monoclonal antibodies against the HLA-DR antigen. In addition, Dendreon retains rights to develop and commercialise its two existing HLA-DR monoclonal antibodies, DN 1921 and DN 1924, as well as other HLA-DR antibodies not being developed by Kirin.Previously, in May 1999, Dendreon and Kirin established a collaboration for the development of dendritic cell-based immunotherapeutics for cancer, including Sipuleucel-T. Under the agreement, Kirin would provide financial support for Dendreon's research on dendritic cells focused on developing immunotherapies for cancers most prevalent in Asia. Dendreon would retain US rights to products arising from the collaboration while Kirin would hold the rights to such immuno-therapeutics in Asia and Oceania.In August 2005, Dendreon signed an agreement to lease a commercial manufacturing facility in Hanover, New Jersey, USA. The company intends to develop the facility to meet anticipated clinical and commercial demands of Sipuleucel-T as well as other active immunotherapy product candidates.Dendreon and Diosynth Biotechnology (Akzo Nobel) have an agreement for the commercial production of the PA 2024 antigen component of Sipuleucel-T. In November 2003,

Dendreon announced that Diosynth successfully manufactured PA 2024 on a commercial scale.In October 2001, Dendreon announced that Gambro Healthcare Inc. would provide a network of centres for cell collection to support commercial production and clinical development of various Dendreon vaccines, including Sipuleucel-T.Dendreon has outsourced its cell processing operations in Mountain View, California, USA to Progenitor Cell Therapy under an amended agreement signed in August 2002. This agreement is an expansion of an existing agreement, under which Progenitor provided Dendreon with cell-processing services through its facility in Hackensack, New Jersey, USA.The pivotal, two-stage, phase III trial (D9902 study) has been initiated at clinical sites in the US. The first stage of the trial (D9902A study) is a double-blind, placebo-controlled phase III trial designed to evaluate Sipuleucel-T in men with asymptomatic, metastatic, androgen-independent prostate cancer. The trial was originally designed to be the companion study to a previously completed phase III trial, called D9901. However, the D9902A study with 98 patients recruited was halted in December 2002, when analysis of the D9901 study revealed no statistically significant benefit in time to disease progression in the overall group, although a benefit was seen in a subgroup of patients with Gleason scores of </=7. In April 2002, the US FDA requested clarification regarding cellular composition of Sipuleucel-T and the suspension of additional patient enrolment for the D9902 study; the request was related solely to manufacturing issues without patient safety being an issue. Trial enrolment resumed in October 2002 following FDA authorisation. Dendreon amended the protocol for the D9902 study and is only recruiting patients with asymptomatic, metastatic, androgen-independent prostate cancer, regardless of their Gleason Score (D9902B study). The ongoing pivotal phase I

Record Date Created: 20060606

**4/9/2 (Item 2 from file: 155)**

DIALOG(R)File 155:MEDLINE(R)



19998843 PMID: 16115700

**Safety and immunological efficacy of a prostate cancer plasmid DNA vaccine encoding prostatic acid phosphatase (PAP).**

Johnson Laura E; Frye Thomas P; Arnot Alana R; Marquette Carrie; Couture Larry A; Gendron-Fitzpatrick Annette; McNeel Douglas G

Department of Medicine, Section of Medical Oncology, University of Wisconsin-Madison, K4/518 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792, USA.

Vaccine (Netherlands) Jan 16 2006, 24 (3) p293-303, ISSN 0264-410X --Print Journal Code: 8406899

Contract/Grant No.: K23 RR16489; RR; NCRR

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

Prostatic acid phosphatase (PAP) is a prostate tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clinical benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat PAP can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunological efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human PAP, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-week intervals with 100, 500, or 1,500 microg

pTVG-HP with 5 microg recombinant rat GM-CSF protein given as a vaccine adjuvant. An additional 12 male Lewis rats served as controls with groups immunized with 1,500 microg of a parental DNA vector not encoding human PAP, and a group that received GM-CSF protein only without plasmid DNA. Groups of animals (n=3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunological analysis. No significant toxicities were observed in terms of animal weights, histopathology, hematological changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically different from control animals. The vaccine was found to be effective in eliciting PAP-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and numbers of immunizations. PAP-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting PAP-specific cellular and humoral immune responses. These findings support the further clinical evaluation of pTVG-HP in patients with prostate cancer.

Tags: Male

Descriptors: *Acid Phosphatase--immunology--IM; *Cancer Vaccines --immunology--IM; *Prostate--enzymology--EN; *Prostate--immunology--IM; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--prevention and control--PC; Animals; Antibody Formation--immunology--IM; Cancer Vaccines --adverse effects--AE; Cancer Vaccines--toxicity--TO; Enzyme-Linked Immunosorbent Assay; Immunity, Cellular--immunology--IM; Immunoglobulin G --biosynthesis--BI; Immunoglobulin G--immunology--IM; Plasmids--immunology --IM; Rats; Rats, Inbred Lew; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Spleen--immunology--IM; T-Lymphocytes--immunology--IM; Vaccines, DNA --adverse effects--AE; Vaccines, DNA--immunology--IM; Vaccines, DNA --toxicity--TO

CAS Registry No.: 0 (Cancer Vaccines); 0 (Immunoglobulin G); 0 (Plasmids); 0 (Vaccines, DNA)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase)

Record Date Created: 20051219

Record Date Completed: 20060227

Date of Electronic Publication: 20050809

**4/9/3 (Item 3 from file: 155)**

DIALOG(R)File 155:MEDLINE(R)



14916534 PMID: 15176049

**Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate cancer: a Phase 2 trial.**

Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir

Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, Minnesota 55902, USA.

Prostate (United States) Aug 1 2004, 60 (3) p197-204, ISSN 0270-4137--Print Journal Code: 8101368

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

BACKGROUND: Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. METHODS: We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. RESULTS: Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. CONCLUSIONS: This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. 

Tags: Male

Descriptors: *Antigen-Presenting Cells--immunology--IM; *Carcinoma --immunology--IM; *Carcinoma--therapy--TH; *Immunotherapy--methods--MT; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--therapy--TH; *Protein-Tyrosine-Phosphatase--genetics--GE; Aged; Aged, 80 and over; Carcinoma--pathology--PA; Granulocyte-Macrophage Colony-Stimulating Factor --administration and dosage--AD; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; Granulocyte-Macrophage Colony-Stimulating Factor --pharmacology--PD; Humans; Infusions, Intravenous; Injections, Subcutaneous; Middle Aged; Neoplasm Metastasis; Prostate-Specific Antigen --analysis--AN; Prostatic Neoplasms--pathology--PA; Protein-Tyrosine-Phosph atase--administration and dosage--AD; Protein-Tyrosine-Phosphatase --pharmacology--PD; Recombinant Fusion Proteins; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Treatment Outcome

CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.- (prostatic acid phosphatase); EC 3.1.3.48 (Protein-Tyrosine-Phosphatase); EC 3.4.21.77 (Prostate-Specific Antigen)

Record Date Created: 20040603

Record Date Completed: 20040903

**4/9/4 (Item 4 from file: 155)**

DIALOG(R)File 155:MEDLINE(R)



14576452 PMID: 14609763

**[Cell therapy and prostate cancer]**

Therapie cellulaire et cancer de la prostate.

Eymard Jean-Christophe; Bernard J

Unite fonctionnelle de recherche clinique et de therapie cellulaire, Institut Jean-Godinot, 1. av du general Koenig, 51056 Reims, France. jc.eymard@reims.fnclcc.fr
Bulletin du cancer (France) Aug-Sep 2003, 90 (8-9) p734-43, ISSN 0007-4551--Print Journal Code: 0072416
Publishing Model Print
Document type: Journal Article; Review ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Hormonotherapy is the standard treatment for advanced prostate cancer but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of cancer cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use GM-CSF gene-transduced allogenic cells. The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two prostate antigens have already been used. PSMA evaluated in 130 patients and a fusion protein PAP-GM-CSF (Provenge) in 144 patients. All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to amplify vaccine response and clinical efficacy. John Libbey Eurotext 2003 (63 Refs.)
Tags: Male
Descriptors: *Dendritic Cells--transplantation--TR; *Immunotherapy --methods--MT; *Prostate-Specific Antigen--immunology--IM; *Prostatic Neoplasms--therapy--TH; Acid Phosphatase--immunology--IM; Antigen-Presenting Cells--immunology--IM; Antigen-Presenting Cells--transplantation--TR; Antigens, Surface--immunology--IM; Cancer Vaccines--immunology--IM; Cell Movement; Clinical Trials, Phase I; Dendritic Cells--immunology--IM; English Abstract; Glutamate Carboxypeptidase II--immunology--IM; Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans; Immunity, Cellular; Major Histocompatibility Complex--immunology--IM; Prostate--enzymology--EN; Prostatic Neoplasms--immunology--IM; Recombinant Fusion Proteins--immunology--IM
CAS Registry No.: 0 (Antigens, Surface); 0 (Cancer Vaccines); 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human) ; EC 3.4.21.77 (Prostate-Specific Antigen)
Record Date Created: 20031111
Record Date Completed: 20031204

**4/9/5 (Item 5 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)


12763307 PMID: 10873066
**Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for prostate cancer.**
Burch P A; Breen J K; Buckner J C; Gastineau D A; Kaur J A; Laus R L;

Padley D J; Peshwa M V; Pitot H C; Richardson R L; Smits B J; Sopapan P; Strang G; Valone F H; Vuk-Pavlovic S

Division of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA.

Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Jun 2000, 6 (6) p2175-82, ISSN 1078-0432--Print Journal Code: 9502500

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We attempted to induce therapeutic immunity against prostate-derived tissues in patients suffering from progressive hormone-refractory metastatic prostate carcinoma. Thirteen patients were treated with two infusions, 1 month apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (GM-CSF) and human prostatic acid phosphatase (PAP). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating prostate-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by GM-CSF (P = 0.0004) and PAP (P = 0.0001), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against PAP and GM-CSF. However, antibodies to GM-CSF and, to a much lesser extent, to PAP reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex vivo can induce antigen-specific cellular immunity in prostate cancer patients, warranting further studies of this mode of immunotherapy.

Tags: Male

Descriptors: *Acid Phosphatase--therapeutic use--TU; *Dendritic Cells --immunology--IM; *Granulocyte-Macrophage Colony-Stimulating Factor --therapeutic use--TU; *Immunotherapy--methods--MT; *Prostatic Neoplasms --immunology--IM; *Prostatic Neoplasms--therapy--TH; *Recombinant Fusion Proteins--therapeutic use--TU; Acid Phosphatase--blood--BL; Antigen-Presenting Cells--immunology--IM; Cell Division--immunology--IM; Dose-Response Relationship, Drug; Humans; Injections, Subcutaneous; Prostate; Research Support, Non-U.S. Gov't; T-Lymphocytes--drug effects--DE; T-Lymphocytes --immunology--IM; Time Factors; Transplantation, Autologous

CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.1.3.2 (PA2024 fusion protein, human)

Record Date Created: 20000929

Record Date Completed: 20001207

**4/9/6 (Item 6 from file: 155)**

DIALOG(R)File 155:MEDLINE(R)

12756334 PMID: 10861757

**PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome.**

Ponniah S; Arah I; Alexander R B

Division of Urology, University of Maryland School of Medicine, and Section of Urology, VA Maryland Health Care System, Baltimore, Maryland 21201, USA. sponniah@smail.umaryland.edu

Prostate (UNITED STATES) Jun 15 2000, 44 (1) p49-54, ISSN 0270-4137 --Print Journal Code: 8101368

Contract/Grant No.: R01-DK53732; DK; NIDDK

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

BACKGROUND: Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the prostate could be candidate antigens in autoimmune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. METHODS: Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by density gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. RESULTS: In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (PAP) or beta-microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. CONCLUSIONS: The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic cancer. 

Tags: Male

Descriptors: *Autoimmune Diseases--immunology--IM; *Pelvic Pain --immunology--IM; *Prostate-Specific Antigen--immunology--IM; *Prostatitis --immunology--IM; Adult; Aged; CD4-Positive T-Lymphocytes--immunology--IM; Cell Division; Centrifugation, Density Gradient; Chronic Disease; Dendritic Cells--immunology--IM; Flow Cytometry; Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans; Immunomagnetic Separation; Interleukin-4--immunology--IM; Microspheres; Middle Aged; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Scintillation Counting; Syndrome

CAS Registry No.: 207137-56-2 (Interleukin-4); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.4.21.77 (Prostate-Specific Antigen)

Record Date Created: 20000710

Record Date Completed: 20000710

**4/9/7 (Item 1 from file: 159)**

DIALOG(R)File 159:Cancerlit


02600878 PMID: 99701197
**Immunotherapy of Hormone Refractory Prostate Cancer (HRPC) with Prostatic Acid Phosphatase (PAP)-Loaded Dendritic Cells (APC8015) (Meeting abstract).**
Valone; Small; Peshwa; Strang; Laus; Ruegg; Schooten W va
University of California, San Francisco, San Francisco, CA.
Proc Annu Meet Am Soc Clin Oncol 1999, 18,
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed
Dendritic cells (DC) are the most potent natural antigen presenting cells (APC) for stimulating immune responses. Twenty-eight men with HRPC were enrolled in a Phase I/II trial of APC8015, prepared and infused intravenously monthly for 3 months. To prepare APC8015, DC precursors are isolated from peripheral leukapheresis products by buoyant density centrifugation and then incubated for 40 hours in serum-free, cytokine-free media with PA2024, which is a fusion protein composed of PAP and a DC targeting element, structurally similar to GM-CSF. Twelve men were treated in a phase I trial of escalating doses of APC8015 (0.2 to 1.2 x 10[Superscript 9] nucleated cells/m[Superscript 2]) and 16 were enrolled in a phase II trial at the maximum dose. Median age was 69 (range: 48-83). Median ECOG performance was 0 (range: 0-1). Median PSA was 63 ng/ml (range: 3.4-1,007). <10% of infusions were associated with mild fevers or myalgias. There were no other treatment-related adverse events. APC8015 induced strong T cell responses to PA2024 in all patients but induced specific antibodies in <20% of patients. IFN<FONT>g but not IL-4 was detected by ELISPOT and ELISA assays suggesting a TH-1 response to PA2024. Antigen-specific T cell precursor frequencies were <1/10[Superscript 5] before treatment and as high as 1/5,000 after treatment. 2 of 22 evaluable patients had >50% decrease in PSA and 4 had a 25-49% decrease (6 too early). Median time to disease progression was 43 weeks in the phase II trial. PAP-loaded DC are safe and effective for stimulating antigen-specific immune responses. Initial phase II data suggest that treatment is clinically active. (C) American Society of Clinical Oncology 1999.
Record Date Created: 19991001

**4/9/8 (Item 1 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0015804453 BIOSIS NO.: 200600149848
**Provenge (R) - Prostate cancer therapy**
AUTHOR: McIntyre J A (Reprint); Fernandez D
AUTHOR ADDRESS: Prous Sci, POB 540, Barcelona 08080, Spain**Spain
JOURNAL: Drugs of the Future 30 (9): p892-895 SEP 2005 2005
ISSN: 0377-8282
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: There are few therapeutic options available for the treatment of hormone-refractory prostate cancer (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing prostate-specific T-cell-mediated immunity. Provenge((R)) (APC-8015) is an

immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (PAP), an antigen found in 95% of prostate cancers, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Early clinical studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge((R)), with increases in prostate-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

REGISTRY NUMBERS: 83869-56-1: granulocyte-macrophage colony-stimulating factor; 9001-77-8: prostatic acid phosphatase
ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase
DESCRIPTORS:
MAJOR CONCEPTS: Pharmacology; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: T-cell--immune system, blood and lymphatics
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: hormone refractory prostate cancer {HRPC}--neoplastic disease, reproductive system disease/male, drug therapy
MESH TERMS: Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: prostate-specific antigen {PSA}; vaccines--immunologic-drug, immunostimulant-drug, vaccine; granulocyte-macrophage colony-stimulating factor {GM-CSF}; prostatic acid phosphatase {PAP}; PA2024 fusion protein; provenge--antineoplastic-drug, immunologic-drug, phase II clinical trial
CONCEPT CODES:
02506 Cytology - Animal
02508 Cytology - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
16506 Reproductive system - Pathology
17002 Endocrine - General
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

**4/9/9 (Item 2 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0015000622 BIOSIS NO.: 200400371411
**Immunotherapy (APC8015, Provenge(R)) targeting prostatic acid phosphatase**

**can induce durable remission of metastatic androgen-independent prostate cancer: A phase 2 trial**

AUTHOR: Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir (Reprint)
AUTHOR ADDRESS: Dept OncolDiv Med Oncol, Mayo Clin, Guggenheim 901B,200 1st St SW, Rochester, MN, 55902, USA**USA
AUTHOR E-MAIL ADDRESS: vuk@mayo.edu
JOURNAL: Prostate 60 (3): p197-204 August 1, 2004 2004
MEDIUM: print
ISSN: 0270-4137 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: BACKGROUND. Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. METHODS. We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. RESULTS. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. CONCLUSIONS. This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte-macrophage colony stimulating factor; 9001-77-8: prostatic acid phosphatase
ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--male, American
ORGANISMS: PARTS ETC: B cell--blood and lymphatics, immune system; CD54 positive cell--immune system; T cell--blood and lymphatics, immune system; antigen-presenting cell--immune system, intravenous infusion;

macrophage--blood and lymphatics, immune system; monocyte--blood and lymphatics, immune system; peripheral blood mononuclear cell {PBMC}--blood and lymphatics, immune system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: androgen-independent prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease, therapy; metastatic retroperitoneal adenopathy--disease-miscellaneous; pelvic adenopathy--disease-miscellaneous; prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease, diagnosis, therapy
MESH TERMS: Prostatic Neoplasms (MeSH); Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: PA2024 fusion protein; Provenge {APC8015}--antineoplastic-drug, immunologic-drug, immunostimulant-drug, phase II clinical trial; granulocyte-macrophage colony stimulating factor {GM-CSF}; prostate-specific antigen; prostatic acid phosphatase
METHODS & EQUIPMENT: computed tomography scan--clinical techniques, diagnostic techniques, imaging and microscopy techniques, laboratory techniques; immunotherapy--clinical techniques, immunologic techniques, laboratory techniques, therapeutic and prophylactic techniques; radionuclide bone scan--clinical techniques, diagnostic techniques
MISCELLANEOUS TERMS: National Cancer Institute {NCI}; National Cancer Institute common toxicity criteria grade 1-4 {NCI common toxicity criteria grade 1-4}; immune response
CONCEPT CODES:
02506 Cytology - Animal
02508 Cytology - Human
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
12504 Pathology - Diagnostic
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
15506 Urinary system - Pathology
16506 Reproductive system - Pathology
17002 Endocrine - General
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24001 Neoplasms - Diagnostic methods
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

**4/9/10 (Item 3 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0013557956 BIOSIS NO.: 200200151467
**Stability characterization of antigen-loaded dendritic cell vaccines**
AUTHOR: Nevin Barry (Reprint); Therond Judy; Ishisaka Toshiye (Reprint); Shiomoto Clifford; Kothari Sudesh S (Reprint); Galie Brian; Yumiaco Orlando Jr; Westerman Rick; Terral Annette; Peshwa Madhusudan V (Reprint)
AUTHOR ADDRESS: Cell Process Development, Dendreon, Seattle, WA, USA**USA
JOURNAL: Blood 98 (11 Part 2): p38b November 16, 2001 2001
MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: ProvengeTM, an immunotherapy product consisting of autologous dendritic cells (DC) loaded ex vivo with a recombinant engineered prostate tumor-antigen (PA2024) consisting of prostatic acid phosphatase (PAP) fused to granulocyte macrophage colony stimulating factor (GM-CSF), is currently in phase III clinical evaluation for treatment of hormone refractory prostate cancer. The patients leukapheresis product was shipped to Dendreon's cGMP cell processing centers where it was processed to enrich dendritic cells, incubated with PA2024 for 36-44 hours, then harvested and formulated in Lactated Ringer's solution for injection, USP and returned to the clinical site for administration. Stability studies were designed wherein the final DC vaccine product was stored refrigerated at 2-8degreeC and samples were analyzed at 0, 8, 12, 24, 30 and 36 hours post-formulation. Samples were characterized for nucleated cell number, cell viability, phenotype, potency, and allogeneic and autologous T cell stimulatory capacity. The dendritic cell fraction was characterized for expression of a variety of co-stimulatory molecules including CD1a, CD11c, CD40, CD54, CD80, CD83, CD86, CD123, HLA-DR, and HLA-A,B,C. Results indicate that there is no difference in any of the product characteristics between 0 and 8 hours. Beyond 8 hours there was no difference in cell viability and phenotype over the stability period evaluated. There was approximately a 10-20% decrease in cell number, potency and T cell stimulatory capacity over a course of 36 hours. The implications of the observed in vitro results on in vivo potency will be discussed.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte macrophage colony stimulating factor
DESCRIPTORS:
MAJOR CONCEPTS: Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS, ETC: T cell--blood and lymphatics, immune system; dendritic cells--immune system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease
MESH TERMS: Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: Provenge--antineoplastic-drug, immunologic-drug, stability, vaccine; granulocyte macrophage colony stimulating factor; prostate tumor-antigen; prostatic acid phosphatase
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02506 Cytology - Animal
02508 Cytology - Human
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
15506 Urinary system - Pathology

16506 Reproductive system - Pathology
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

**4/9/11 (Item 1 from file: 73)**
DIALOG(R)File 73:EMBASE


13316952 EMBASE No: 2005387607
**Session II: Tumor antigens - Prostate cancer antigens and vaccines**
Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.; Belldegrun A.; Logothetis C.; Papandreou C.
Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA United States
Cancer Immunology, Immunotherapy ( CANCER IMMUNOL. IMMUNOTHER. ) (Germany) 2003, 52/SUPPL. 1 (S8-S9+S27)
CODEN: CIIMD ISSN: 0340-7004
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The clinical development of prostate cancer vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those cancers for which tumor and immune cells are readily available. Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory prostate cancer (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate cancer: prostate-specific membrane antigen (PSMA), prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and PAP as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (GM-CSF, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC

at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. 

DRUG DESCRIPTORS:
*tumor antigen; *cancer vaccine--adverse drug reaction--ae; *cancer vaccine --clinical trial--ct; *cancer vaccine--drug therapy--dt
tumor rejection antigen; tumor suppressor protein; prostate antigen; acid phosphatase prostate isoenzyme; prostate specific antigen; prostate specific membrane antigen--drug therapy--dt; prostate specific membrane antigen--intradermal drug administration--dl; prostate specific membrane antigen--pharmacology--pd; recombinant antigen--drug therapy--dt; recombinant antigen--intradermal drug administration--dl; recombinant antigen--pharmacology--pd; dendritic cell vaccine--adverse drug reaction --ae; dendritic cell vaccine--clinical trial--ct; dendritic cell vaccine --drug therapy--dt
MEDICAL DESCRIPTORS:
*prostate cancer--drug therapy--dt
prostatectomy; cancer surgery; bone metastasis; cancer cell culture; T lymphocyte; medical research; cancer chemotherapy; immune response; cancer survival; quality of life; dendritic cell; peripheral blood mononuclear cell; skin irritation--side effect--si; injection site reaction--side effect--si; headache--side effect--si; fatigue--side effect--si; human; clinical trial; conference paper; priority journal
SECTION HEADINGS:
  016 Cancer
  026 Immunology, Serology and Transplantation
  028 Urology and Nephrology
  037 Drug Literature Index
  038 Adverse Reaction Titles
?

| Set | Items | Description |
|---|---|---|
| S1 | 137 | (PSA AND (GM (W) CSF) AND PROSTATE) |
| S2 | 65 | RD S1 (unique items) |
| S3 | 28 | (PAP AND (GM (W) CSF) AND PROSTATE) |
| S4 | 11 | RD S3 (unique items) |

?


| Set | Items | Description |
|---|---|---|
| S1 | 137 | (PSA AND (GM (W) CSF) AND PROSTATE) |
| S2 | 65 | RD S1 (unique items) |
| S3 | 28 | (PAP AND (GM (W) CSF) AND PROSTATE) |
| S4 | 11 | RD S3 (unique items) |


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S (PAP AND (GM (W) CSF) AND CANCER)
           38783  PAP
          137699  GM
          234248  CSF
           60986  GM(W)CSF
         3460920  CANCER
      S5      35  (PAP AND (GM (W) CSF) AND CANCER)
?

RD S5
      S6      18  RD S5  (unique items)
?

TYPE S6/FULL/1-18

  6/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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20889595   PMID: 16752945
 Sipuleucel-T: APC 8015, APC-8015, Prostate Cancer Vaccine - Dendreon.
  Drugs in R&D (New Zealand)    2006, 7 (3) p197-201, ISSN 1174-5886--
Print   Journal Code: 100883647
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: In Data Review
  Subfile:   INDEX MEDICUS
  Sipuleucel-T [APC 8015, Provenge((R))] is an autologous, dendritic
cell-based vaccine under development with Dendreon Corporation for the
treatment of androgen-independent and androgen-dependent prostate cancer.
It was generated using the company's active immunotherapy platform to
stimulate a patient's own immune system to specifically target and destroy
cancer cells, while leaving healthy cells unharmed. This approach could
provide patients with a meaningful survival benefit and an improved
tolerability profile over exisiting anticancer therapies. Sipuleucel-T
selectively targets the prostate-specific antigen (PSA) known as prostatic
acid phosphatase (PAP) that is expressed in approximate, equals95% of
prostate cancers. It is produced by ex vivo exposure of dendritic cell
precursors to PA 2024, a recombinant fusion protein composed of the PAP
target fused to granulocyte-macrophage colony-stimulating factor (GM-CSF)
and incorporated into Dendreon's proprietary Antigen Delivery Cassettetrade
mark. Patients are typically administered three intravenous (IV)-infusions
of the vaccine over a 1-month period as a complete course of therapy. It is
undergoing late-stage clinical evaluation among patients with early and
advanced prostate cancer.In November 2003, Kirin Brewery returned to
Dendreon the full rights to Sipuleucel-T for Asia. In exchange, Dendreon
licensed patent rights relating to the use of certain HLA-DR antibodies to
Kirin for $US20 million. This amended agreement enables Dendreon to
complete ongoing discussions for a worldwide marketing and sales
partnership for Sipuleucel-T. Similarly, Kirin is able to develop its
HLA-DR monoclonal antibodies free of potential infringement claims arising
from Dendreon's patent rights to HLA-DR. The licensing agreement relates to
patent rights owned by Dendreon relating to monoclonal antibodies against
the HLA-DR antigen. In addition, Dendreon retains rights to develop and
commercialise its two existing HLA-DR monoclonal antibodies, DN 1921 and DN
1924, as well as other HLA-DR antibodies not being developed by
Kirin.Previously, in May 1999, Dendreon and Kirin established a
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collaboration for the development of dendritic cell-based immunotherapeutics for cancer, including Sipuleucel-T. Under the agreement, Kirin would provide financial support for Dendreon's research on dendritic cells focused on developing immunotherapies for cancers most prevalent in Asia. Dendreon would retain US rights to products arising from the collaboration while Kirin would hold the rights to such immuno-therapeutics in Asia and Oceania.In August 2005, Dendreon signed an agreement to lease a commercial manufacturing facility in Hanover, New Jersey, USA. The company intends to develop the facility to meet anticipated clinical and commercial demands of Sipuleucel-T as well as other active immunotherapy product candidates.Dendreon and Diosynth Biotechnology (Akzo Nobel) have an agreement for the commercial production of the PA 2024 antigen component of Sipuleucel-T. In November 2003, Dendreon announced that Diosynth successfully manufactured PA 2024 on a commercial scale.In October 2001, Dendreon announced that Gambro Healthcare Inc. would provide a network of centres for cell collection to support commercial production and clinical development of various Dendreon vaccines, including Sipuleucel-T.Dendreon has outsourced its cell processing operations in Mountain View, California, USA to Progenitor Cell Therapy under an amended agreement signed in August 2002. This agreement is an expansion of an existing agreement, under which Progenitor provided Dendreon with cell-processing services through its facility in Hackensack, New Jersey, USA.The pivotal, two-stage, phase III trial (D9902 study) has been initiated at clinical sites in the US. The first stage of the trial (D9902A study) is a double-blind, placebo-controlled phase III trial designed to evaluate Sipuleucel-T in men with asymptomatic, metastatic, androgen-independent prostate cancer. The trial was originally designed to be the companion study to a previously completed phase III trial, called D9901. However, the D9902A study with 98 patients recruited was halted in December 2002, when analysis of the D9901 study revealed no statistically significant benefit in time to disease progression in the overall group, although a benefit was seen in a subgroup of patients with Gleason scores of </=7. In April 2002, the US FDA requested clarification regarding cellular composition of Sipuleucel-T and the suspension of additional patient enrolment for the D9902 study; the request was related solely to manufacturing issues without patient safety being an issue. Trial enrolment resumed in October 2002 following FDA authorisation. Dendreon amended the protocol for the D9902 study and is only recruiting patients with asymptomatic, metastatic, androgen-independent prostate cancer, regardless of their Gleason Score (D9902B study). The ongoing pivotal phase I

Record Date Created: 20060606

**6/9/2 (Item 2 from file: 155)**

DIALOG(R)File 155:MEDLINE(R)



19998843 PMID: 16115700

**Safety and immunological efficacy of a prostate cancer plasmid DNA vaccine encoding prostatic acid phosphatase (PAP).**

Johnson Laura E; Frye Thomas P; Arnot Alana R; Marquette Carrie; Couture Larry A; Gendron-Fitzpatrick Annette; McNeel Douglas G

Department of Medicine, Section of Medical Oncology, University of Wisconsin-Madison, K4/518 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792, USA.

Vaccine (Netherlands) Jan 16 2006, 24 (3) p293-303, ISSN 0264-410X --Print Journal Code: 8406899

Contract/Grant No.: K23 RR16489; RR; NCRR

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS; Toxbib

Prostatic acid phosphatase (PAP) is a prostate tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clinical benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat PAP can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunological efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human PAP, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-week intervals with 100, 500, or 1,500 microg pTVG-HP with 5 microg recombinant rat GM-CSF protein given as a vaccine adjuvant. An additional 12 male Lewis rats served as controls with groups immunized with 1,500 microg of a parental DNA vector not encoding human PAP, and a group that received GM-CSF protein only without plasmid DNA. Groups of animals (n=3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunological analysis. No significant toxicities were observed in terms of animal weights, histopathology, hematological changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically different from control animals. The vaccine was found to be effective in eliciting PAP-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and numbers of immunizations. PAP-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting PAP-specific cellular and humoral immune responses. These findings support the further clinical evaluation of pTVG-HP in patients with prostate cancer.

Tags: Male
Descriptors: *Acid Phosphatase--immunology--IM; *Cancer Vaccines --immunology--IM; *Prostate--enzymology--EN; *Prostate--immunology--IM; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--prevention and control--PC; Animals; Antibody Formation--immunology--IM; Cancer Vaccines --adverse effects--AE; Cancer Vaccines--toxicity--TO; Enzyme-Linked Immunosorbent Assay; Immunity, Cellular--immunology--IM; Immunoglobulin G --biosynthesis--BI; Immunoglobulin G--immunology--IM; Plasmids--immunology --IM; Rats; Rats, Inbred Lew; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Spleen--immunology--IM; T-Lymphocytes--immunology--IM; Vaccines, DNA --adverse effects--AE; Vaccines, DNA--immunology--IM; Vaccines, DNA --toxicity--TO
CAS Registry No.: 0 (Cancer Vaccines); 0 (Immunoglobulin G); 0 (Plasmids); 0 (Vaccines, DNA)
Enzyme No.: EC 3.1.3.2 (Acid Phosphatase)
Record Date Created: 20051219
Record Date Completed: 20060227
Date of Electronic Publication: 20050809

**6/9/3 (Item 3 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)
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14916534 PMID: 15176049
**Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate**

**cancer: a Phase 2 trial.**

Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir

Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, Minnesota 55902, USA.

Prostate (United States) Aug 1 2004, 60 (3) p197-204, ISSN 0270-4137--Print Journal Code: 8101368

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

BACKGROUND: Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. METHODS: We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. RESULTS: Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. CONCLUSIONS: This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

Tags: Male

Descriptors: *Antigen-Presenting Cells--immunology--IM; *Carcinoma --immunology--IM; *Carcinoma--therapy--TH; *Immunotherapy--methods--MT; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--therapy--TH; *Protein-Tyrosine-Phosphatase--genetics--GE; Aged; Aged, 80 and over; Carcinoma--pathology--PA; Granulocyte-Macrophage Colony-Stimulating Factor --administration and dosage--AD; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; Granulocyte-Macrophage Colony-Stimulating Factor --pharmacology--PD; Humans; Infusions, Intravenous; Injections, Subcutaneous; Middle Aged; Neoplasm Metastasis; Prostate-Specific Antigen --analysis--AN; Prostatic Neoplasms--pathology--PA; Protein-Tyrosine-Phosph atase--administration and dosage--AD; Protein-Tyrosine-Phosphatase --pharmacology--PD; Recombinant Fusion Proteins; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Treatment Outcome

CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.- (prostatic acid phosphatase); EC 3.1.3.48

(Protein-Tyrosine-Phosphatase); EC 3.4.21.77 (Prostate-Specific Antigen)
Record Date Created: 20040603
Record Date Completed: 20040903

**6/9/4 (Item 4 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)


14576452 PMID: 14609763
**[Cell therapy and prostate cancer]**
Therapie cellulaire et cancer de la prostate.
Eymard Jean-Christophe; Bernard J
Unite fonctionnelle de recherche clinique et de therapie cellulaire, Institut Jean-Godinot, 1. av du general Koenig, 51056 Reims, France. jc.eymard@reims.fnclcc.fr
Bulletin du cancer (France) Aug-Sep 2003, 90 (8-9) p734-43, ISSN 0007-4551--Print Journal Code: 0072416
Publishing Model Print
Document type: Journal Article; Review ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Hormonotherapy is the standard treatment for advanced prostate cancer but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of cancer cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use GM-CSF gene-transduced allogenic cells. The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two prostate antigens have already been used. PSMA evaluated in 130 patients and a fusion protein PAP-GM-CSF (Provenge) in 144 patients. All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to amplify vaccine response and clinical efficacy. John Libbey Eurotext 2003 (63 Refs.)
Tags: Male
Descriptors: *Dendritic Cells--transplantation--TR; *Immunotherapy --methods--MT; *Prostate-Specific Antigen--immunology--IM; *Prostatic Neoplasms--therapy--TH; Acid Phosphatase--immunology--IM; Antigen-Presenting Cells--immunology--IM; Antigen-Presenting Cells--transplantation--TR; Antigens, Surface--immunology--IM; Cancer Vaccines--immunology--IM; Cell Movement; Clinical Trials, Phase I; Dendritic Cells--immunology--IM; English Abstract; Glutamate Carboxypeptidase II--immunology--IM; Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans; Immunity, Cellular; Major Histocompatibility Complex--immunology--IM; Prostate--enzymology--EN; Prostatic Neoplasms--immunology--IM; Recombinant Fusion Proteins--immunology--IM
CAS Registry No.: 0 (Antigens, Surface); 0 (Cancer Vaccines); 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.4.17.21 (Glutamate Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)

; EC 3.4.21.77 (Prostate-Specific Antigen)
Record Date Created: 20031111
Record Date Completed: 20031204

**6/9/5 (Item 5 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)


12763307 PMID: 10873066
**Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for prostate cancer.**
Burch P A; Breen J K; Buckner J C; Gastineau D A; Kaur J A; Laus R L; Padley D J; Peshwa M V; Pitot H C; Richardson R L; Smits B J; Sopapan P; Strang G; Valone F H; Vuk-Pavlovic S
Division of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA.
Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Jun 2000, 6 (6) p2175-82, ISSN 1078-0432--Print Journal Code: 9502500
Publishing Model Print
Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
We attempted to induce therapeutic immunity against prostate-derived tissues in patients suffering from progressive hormone-refractory metastatic prostate carcinoma. Thirteen patients were treated with two infusions, 1 month apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (GM-CSF) and human prostatic acid phosphatase (PAP). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating prostate-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by GM-CSF (P = 0.0004) and PAP (P = 0.0001), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against PAP and GM-CSF. However, antibodies to GM-CSF and, to a much lesser extent, to PAP reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex vivo can induce antigen-specific cellular immunity in prostate cancer patients, warranting further studies of this mode of immunotherapy.
Tags: Male
Descriptors: *Acid Phosphatase--therapeutic use--TU; *Dendritic Cells --immunology--IM; *Granulocyte-Macrophage Colony-Stimulating Factor --therapeutic use--TU; *Immunotherapy--methods--MT; *Prostatic Neoplasms --immunology--IM; *Prostatic Neoplasms--therapy--TH; *Recombinant Fusion Proteins--therapeutic use--TU; Acid Phosphatase--blood--BL; Antigen-Presenting Cells--immunology--IM; Cell Division--immunology--IM; Dose-Response Relationship, Drug; Humans; Injections, Subcutaneous; Prostate; Research Support, Non-U.S. Gov't; T-Lymphocytes--drug effects--DE; T-Lymphocytes

--immunology--IM; Time Factors; Transplantation, Autologous
CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.1.3.2 (PA2024 fusion protein, human)
Record Date Created: 20000929
Record Date Completed: 20001207

**6/9/6 (Item 6 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)


12756334 PMID: 10861757
**PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome.**
Ponniah S; Arah I; Alexander R B
Division of Urology, University of Maryland School of Medicine, and Section of Urology, VA Maryland Health Care System, Baltimore, Maryland 21201, USA. sponniah@smail.umaryland.edu
Prostate (UNITED STATES) Jun 15 2000, 44 (1) p49-54, ISSN 0270-4137 --Print Journal Code: 8101368
Contract/Grant No.: R01-DK53732; DK; NIDDK
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
BACKGROUND: Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the prostate could be candidate antigens in autoimmune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. METHODS: Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by density gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. RESULTS: In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (PAP) or beta-microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. CONCLUSIONS: The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic cancer. Copyright 2000 Wiley-Liss, Inc.
Tags: Male
Descriptors: *Autoimmune Diseases--immunology--IM; *Pelvic Pain --immunology--IM; *Prostate-Specific Antigen--immunology--IM; *Prostatitis --immunology--IM; Adult; Aged; CD4-Positive T-Lymphocytes--immunology--IM; Cell Division; Centrifugation, Density Gradient; Chronic Disease; Dendritic

Cells--immunology--IM; Flow Cytometry; Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans; Immunomagnetic Separation; Interleukin-4--immunology--IM; Microspheres; Middle Aged; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Scintillation Counting; Syndrome
CAS Registry No.: 207137-56-2 (Interleukin-4); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
Enzyme No.: EC 3.4.21.77 (Prostate-Specific Antigen)
Record Date Created: 20000710
Record Date Completed: 20000710

**6/9/7 (Item 1 from file: 159)**
DIALOG(R)File 159:Cancerlit
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02600878 PMID: 99701197
**Immunotherapy of Hormone Refractory Prostate Cancer (HRPC) with Prostatic Acid Phosphatase (PAP)-Loaded Dendritic Cells (APC8015) (Meeting abstract).**
Valone; Small; Peshwa; Strang; Laus; Ruegg; Schooten W va
University of California, San Francisco, San Francisco, CA.
Proc Annu Meet Am Soc Clin Oncol 1999, 18,
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed
Dendritic cells (DC) are the most potent natural antigen presenting cells (APC) for stimulating immune responses. Twenty-eight men with HRPC were enrolled in a Phase I/II trial of APC8015, prepared and infused intravenously monthly for 3 months. To prepare APC8015, DC precursors are isolated from peripheral leukapheresis products by buoyant density centrifugation and then incubated for 40 hours in serum-free, cytokine-free media with PA2024, which is a fusion protein composed of PAP and a DC targeting element, structurally similar to GM-CSF. Twelve men were treated in a phase I trial of escalating doses of APC8015 (0.2 to 1.2 x 10[Superscript 9] nucleated cells/m[Superscript 2]) and 16 were enrolled in a phase II trial at the maximum dose. Median age was 69 (range: 48-83). Median ECOG performance was 0 (range: 0-1). Median PSA was 63 ng/ml (range: 3.4-1,007). <10% of infusions were associated with mild fevers or myalgias. There were no other treatment-related adverse events. APC8015 induced strong T cell responses to PA2024 in all patients but induced specific antibodies in <20% of patients. IFN<FONT>g but not IL-4 was detected by ELISPOT and ELISA assays suggesting a TH-1 response to PA2024. Antigen-specific T cell precursor frequencies were <1/10[Superscript 5] before treatment and as high as 1/5,000 after treatment. 2 of 22 evaluable patients had >50% decrease in PSA and 4 had a 25-49% decrease (6 too early). Median time to disease progression was 43 weeks in the phase II trial. PAP-loaded DC are safe and effective for stimulating antigen-specific immune responses. Initial phase II data suggest that treatment is clinically active. (C) American Society of Clinical Oncology 1999.
Record Date Created: 19991001

**6/9/8 (Item 1 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)
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0015804453 BIOSIS NO.: 200600149848
**Provenge (R) - Prostate cancer therapy**

AUTHOR: McIntyre J A (Reprint); Fernandez D
AUTHOR ADDRESS: Prous Sci, POB 540, Barcelona 08080, Spain**Spain
JOURNAL: Drugs of the Future 30 (9): p892-895 SEP 2005 2005
ISSN: 0377-8282
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: There are few therapeutic options available for the treatment of hormone-refractory prostate cancer (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing prostate-specific T-cell-mediated immunity. Provenge((R)) (APC-8015) is an immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (PAP), an antigen found in 95% of prostate cancers, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Early clinical studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge((R)), with increases in prostate-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

REGISTRY NUMBERS: 83869-56-1: granulocyte-macrophage colony-stimulating factor; 9001-77-8: prostatic acid phosphatase
ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase
DESCRIPTORS:
MAJOR CONCEPTS: Pharmacology; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: T-cell--immune system, blood and lymphatics
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: hormone refractory prostate cancer {HRPC}--neoplastic disease, reproductive system disease/male, drug therapy
MESH TERMS: Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: prostate-specific antigen {PSA}; vaccines--immunologic-drug, immunostimulant-drug, vaccine; granulocyte-macrophage colony-stimulating factor {GM-CSF}; prostatic acid phosphatase {PAP}; PA2024 fusion protein; provenge--antineoplastic-drug, immunologic-drug, phase II clinical trial
CONCEPT CODES:
02506 Cytology - Animal
02508 Cytology - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
16506 Reproductive system - Pathology
17002 Endocrine - General
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects

24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

**6/9/9 (Item 2 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0015000622 BIOSIS NO.: 200400371411
**Immunotherapy (APC8015, Provenge(R)) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate cancer: A phase 2 trial**
AUTHOR: Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir (Reprint)
AUTHOR ADDRESS: Dept OncolDiv Med Oncol, Mayo Clin, Guggenheim 901B,200 1st St SW, Rochester, MN, 55902, USA**USA
AUTHOR E-MAIL ADDRESS: vuk@mayo.edu
JOURNAL: Prostate 60 (3): p197-204 August 1, 2004 2004
MEDIUM: print
ISSN: 0270-4137 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: BACKGROUND. Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. METHODS. We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. RESULTS. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. CONCLUSIONS. This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte-macrophage

colony stimulating factor; 9001-77-8: prostatic acid phosphatase
ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--male, American
ORGANISMS: PARTS ETC: B cell--blood and lymphatics, immune system; CD54 positive cell--immune system; T cell--blood and lymphatics, immune system; antigen-presenting cell--immune system, intravenous infusion; macrophage--blood and lymphatics, immune system; monocyte--blood and lymphatics, immune system; peripheral blood mononuclear cell {PBMC}--blood and lymphatics, immune system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: androgen-independent prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease, therapy; metastatic retroperitoneal adenopathy--disease-miscellaneous; pelvic adenopathy--disease-miscellaneous; prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease, diagnosis, therapy
MESH TERMS: Prostatic Neoplasms (MeSH); Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: PA2024 fusion protein; Provenge {APC8015}--antineoplastic-drug, immunologic-drug, immunostimulant-drug, phase II clinical trial; granulocyte-macrophage colony stimulating factor {GM-CSF}; prostate-specific antigen; prostatic acid phosphatase
METHODS & EQUIPMENT: computed tomography scan--clinical techniques, diagnostic techniques, imaging and microscopy techniques, laboratory techniques; immunotherapy--clinical techniques, immunologic techniques, laboratory techniques, therapeutic and prophylactic techniques; radionuclide bone scan--clinical techniques, diagnostic techniques
MISCELLANEOUS TERMS: National Cancer Institute {NCI}; National Cancer Institute common toxicity criteria grade 1-4 {NCI common toxicity criteria grade 1-4}; immune response
CONCEPT CODES:
02506 Cytology - Animal
02508 Cytology - Human
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
12504 Pathology - Diagnostic
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
15506 Urinary system - Pathology
16506 Reproductive system - Pathology
17002 Endocrine - General
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24001 Neoplasms - Diagnostic methods
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

6/9/10 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


0013557956 BIOSIS NO.: 200200151467
**Stability characterization of antigen-loaded dendritic cell vaccines**
AUTHOR: Nevin Barry (Reprint); Therond Judy; Ishisaka Toshiye (Reprint); Shiomoto Clifford; Kothari Sudesh S (Reprint); Galie Brian; Yumiaco Orlando Jr; Westerman Rick; Terral Annette; Peshwa Madhusudan V (Reprint)
AUTHOR ADDRESS: Cell Process Development, Dendreon, Seattle, WA, USA**USA
JOURNAL: Blood 98 (11 Part 2): p38b November 16, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: ProvengeTM, an immunotherapy product consisting of autologous dendritic cells (DC) loaded ex vivo with a recombinant engineered prostate tumor-antigen (PA2024) consisting of prostatic acid phosphatase (PAP) fused to granulocyte macrophage colony stimulating factor (GM-CSF), is currently in phase III clinical evaluation for treatment of hormone refractory prostate cancer. The patients leukapheresis product was shipped to Dendreon's cGMP cell processing centers where it was processed to enrich dendritic cells, incubated with PA2024 for 36-44 hours, then harvested and formulated in Lactated Ringer's solution for injection, USP and returned to the clinical site for administration. Stability studies were designed wherein the final DC vaccine product was stored refrigerated at 2-8degreeC and samples were analyzed at 0, 8, 12, 24, 30 and 36 hours post-formulation. Samples were characterized for nucleated cell number, cell viability, phenotype, potency, and allogeneic and autologous T cell stimulatory capacity. The dendritic cell fraction was characterized for expression of a variety of co-stimulatory molecules including CD1a, CD11c, CD40, CD54, CD80, CD83, CD86, CD123, HLA-DR, and HLA-A,B,C. Results indicate that there is no difference in any of the product characteristics between 0 and 8 hours. Beyond 8 hours there was no difference in cell viability and phenotype over the stability period evaluated. There was approximately a 10-20% decrease in cell number, potency and T cell stimulatory capacity over a course of 36 hours. The implications of the observed in vitro results on in vivo potency will be discussed.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte macrophage colony stimulating factor
DESCRIPTORS:
MAJOR CONCEPTS: Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS ETC: T cell--blood and lymphatics, immune system; dendritic cells--immune system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease

MESH TERMS: Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: Provenge--antineoplastic-drug, immunologic-drug, stability, vaccine; granulocyte macrophage colony stimulating factor; prostate tumor-antigen; prostatic acid phosphatase
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02506 Cytology - Animal
02508 Cytology - Human
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
15506 Urinary system - Pathology
16506 Reproductive system - Pathology
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

**6/9/11 (Item 1 from file: 73)**
DIALOG(R)File 73:EMBASE


13316952 EMBASE No: 2005387607
**Session II: Tumor antigens - Prostate cancer antigens and vaccines**
Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.; Belldegrun A.; Logothetis C.; Papandreou C.
Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA United States
Cancer Immunology, Immunotherapy ( CANCER IMMUNOL. IMMUNOTHER. ) (Germany) 2003, 52/SUPPL. 1 (S8-S9+S27)
CODEN: CIIMD ISSN: 0340-7004
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The clinical development of prostate cancer vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those cancers for which tumor and immune cells are readily available. Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory prostate cancer (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate cancer: prostate-specific membrane antigen (PSMA),

prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and PAP as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (GM-CSF, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. 

DRUG DESCRIPTORS:
*tumor antigen; *cancer vaccine--adverse drug reaction--ae; *cancer vaccine --clinical trial--ct; *cancer vaccine--drug therapy--dt
tumor rejection antigen; tumor suppressor protein; prostate antigen; acid phosphatase prostate isoenzyme; prostate specific antigen; prostate specific membrane antigen--drug therapy--dt; prostate specific membrane antigen--intradermal drug administration--dl; prostate specific membrane antigen--pharmacology--pd; recombinant antigen--drug therapy--dt; recombinant antigen--intradermal drug administration--dl; recombinant antigen--pharmacology--pd; dendritic cell vaccine--adverse drug reaction --ae; dendritic cell vaccine--clinical trial--ct; dendritic cell vaccine --drug therapy--dt
MEDICAL DESCRIPTORS:
*prostate cancer--drug therapy--dt
prostatectomy; cancer surgery; bone metastasis; cancer cell culture; T lymphocyte; medical research; cancer chemotherapy; immune response; cancer survival; quality of life; dendritic cell; peripheral blood mononuclear cell; skin irritation--side effect--si; injection site reaction--side effect--si; headache--side effect--si; fatigue--side effect--si; human; clinical trial; conference paper; priority journal
SECTION HEADINGS:
  016 Cancer
  026 Immunology, Serology and Transplantation
  028 Urology and Nephrology
  037 Drug Literature Index
  038 Adverse Reaction Titles

**6/9/12 (Item 2 from file: 73)**
DIALOG(R)File 73:EMBASE

07378239 EMBASE No: 1998268893

**Defective expression of granulocyte-macrophage colony-stimulating factor/interleukin-3/interleukin-5 receptor common beta chain in children with acute myeloid leukemia associated with respiratory failure**

Dirksen U.; Hattenhorst U.; Schneider P.; Schroten H.; Gobel U.; Bocking A.; Muller K.-M.; Murray R.; Burdach S.
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AUTHOR EMAIL: dirksen@uni-duesseldorf.de

Blood ( BLOOD ) (United States) 15 AUG 1998, 92/4 (1097-1103)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

Deficiency of the granulocyte-macrophage colony-stimulating factor (GM-CSF)/interleukin-3 (IL-3)/IL-5 receptors common beta chain (betac) is a cause of fatal respiratory failure. betac deficiency manifests as pulmonary alveolar proteinosis (PAP). PAP has heterogenous etiologies that may be genetic or aquired. Some cases of PAP have been reported to be associated with hematologic malignancies such as acute myeloid leukemia (AML). in mice, the PAP phenotype was generated by targeted deletion of the gene for betac and can be treated by transplantation of wild-type bone marrow into betac -/- mice. Thus, our findings in betac -/- mice provide evidence for a causal relationship between the lung disease and the hematopoietic system. We describe here expression defects of betac or betac plus GM-CSF receptor alpha chain (GM-CSFR alpha) in 3 pediatric patients with AML and PAP symptoms. All of the patients' leukemic cells failed to express normal levels of betac. The leukemic cells of patients no. 2 and 3 additionally lacked the expression of GM-CSFR alpha, as shown by flow cytometry. Strikingly reduced or absent function of betac was demonstrated in clonogenic progenitor assays with absent colony-forming unit (CFU) growth after GM-CSF or IL-3 stimulation. The response to growth factors acting via a growth factor receptor distinct from the GM-CSF/IL-3/IL-5 system (recombinant human granulocyte colony-stimulating factor [rhG-CSF]) was normal. After antileukemic treatment, the pulmonary symptoms resolved and betac or betac plus GM-CSFR alpha expression was normal. Our findings provide evidence that a defect in the expression of betac or betac plus GM-CSFR alpha on AML blasts can be associated with respiratory failure in patients with AML.

DRUG DESCRIPTORS:
*granulocyte macrophage colony stimulating factor receptor--endogenous compound--ec; *interleukin 3 receptor--endogenous compound--ec; * interleukin 5 receptor--endogenous compound--ec
interleukin 3; interleukin 5; recombinant granulocyte colony stimulating factor; apolipoprotein a--endogenous compound--ec; apolipoprotein b --endogenous compound--ec; antileukemic agent
MEDICAL DESCRIPTORS:
*acute granulocytic leukemia--diagnosis--di; *acute granulocytic leukemia --etiology--et; *acute granulocytic leukemia--radiotherapy--rt; *acute granulocytic leukemia--surgery--su; *respiratory failure--complication--co; *respiratory failure--diagnosis--di; *respiratory failure--etiology--et; * lung alveolus proteinosis--complication--co; *lung alveolus proteinosis --diagnosis--di; *lung alveolus proteinosis--etiology--et
protein expression; flow cytometry; clonogenic assay; colony forming unit; thorax radiography; lung lavage; mononuclear cell; allogenic bone marrow transplantation; cancer chemotherapy; whole body radiation; human; male;

female; case report; controlled study; human cell; infant; school child;
article; priority journal
CAS REGISTRY NO.: 121181-53-1 (recombinant granulocyte colony stimulating
factor)
SECTION HEADINGS:
005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
025 Hematology
029 Clinical and Experimental Biochemistry

**6/9/13 (Item 3 from file: 73)**
DIALOG(R)File 73:EMBASE


06852713 EMBASE No: 1997135313
**Effects of Phytolacca acinosa polysaccharides I with different schedules on its antitumor efficiency in tumor bearing mice and production of IL-1, IL-2, IL-6, TNF, CSF activity in normal mice**
Wang H.-B.; Zheng Q.-W.
H.-B. Wang, Department of Pharmacology, College of Pharmacy, Second Military Medical University, Shanghai 200433 China
Immunopharmacology and Immunotoxicology ( IMMUNOPHARMACOL. IMMUNOTOXICOL. ) (United States) 1997, 19/2 (197-213)
CODEN: IITOE ISSN: 0892-3973
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 29

Effects of Phytolacca acinosa polysaccharides I (PAP-I), 5-40 mg/kg in timing of 7 times/wk, 3 times/wk and 1 time/wk on their antitumor efficiency in Sarcoma-180 bearing mice were comparatively investigated. The results confirmed that PAP-I (10 mg/kg, 3 times/wk) reached its optimal antitumor efficiency. Concanavalin A-, lipopolysaccharides-induced lymphocyte proliferation and the IL-2 production were tested in normal mice which were treated with PAP-I, 5-50 mg/kg in timing of 1 time/wk and 3 times/wk. The results showed that PAP-I could augment lymphocyte proliferation and IL-2 production in the group treated with PAP-I in timing of once a week. However, in the group 3 times/wk, PAP-I could significantly weaken lymphocyte proliferation and IL-2 production. Further studies on IL-1, TNF and IL-6 secreted from macrophages and the level of CSF activity in serum of normal mice with different schedules showed that PAP-I (10 mg/kg, 3 times/wk) was the best one in regulating the production of IL-1, TNF, IL-6 and CSF activity. M-CSF was confirmed in the serum by using monoclonal antibody of IL-3, GM-CSF and polyclonal antibody of M-CSF. These results suggested that the antitumor effect of PAP-I, may be mainly related to its augmenting effect on macrophages in mice.

DRUG DESCRIPTORS:
*interleukin 1--endogenous compound--ec; *interleukin 2--endogenous compound--ec; *interleukin 6--endogenous compound--ec; *plant extract --pharmacology--pd; *plant extract--drug dose--do; *polysaccharide --pharmacology--pd; *polysaccharide--drug dose--do; *tumor necrosis factor --endogenous compound--ec
MEDICAL DESCRIPTORS:
*antineoplastic activity; *macrophage
animal cell; article; intraperitoneal drug administration; mouse; nonhuman; priority journal
CAS REGISTRY NO.: 85898-30-2 (interleukin 2)
SECTION HEADINGS:

016 Cancer
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

6/9/14 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


14931093 Genuine Article#: 021CY Number of References: 50
**Title: Aerosol granulocyte-macrophage colony-stimulating factor for pulmonary alveolar proteinosis**
Author(s): Wylam ME (REPRINT) ; Ten R; Prakash UBS; Nadrous HF; Clawson ML; Anderson PM
Corporate Source: Mayo Clin,Coll Med, Dept Internal Med & Paediat,200 1st St,SW/Rochester//MN/55905 (REPRINT); Mayo Clin,Coll Med, Dept Internal Med & Paediat,Rochester//MN/55905(wylam.mark@mayo.edu)
Journal: EUROPEAN RESPIRATORY JOURNAL, 2006, V27, N3 (MAR), P585-593
ISSN: 0903-1936 Publication date: 20060300
Publisher: EUROPEAN RESPIRATORY SOC JOURNALS LTD, 146 WEST ST, STE 2.4, HUTTONS BLDG, SHEFFIELD S1 4ES, ENGLAND
Language: English Document Type: ARTICLE
Geographic Location: USA
Journal Subject Category: RESPIRATORY SYSTEM
Abstract: Recently, granulocyte-macrophage colony-stimulating factor (GM-CSF) autoantibodies have been found in many patients with pulmonary alveolar proteinosis (PAP). The present study reports a retrospective case series of patients who used aerosolised GM-CSF in the treatment of idiopathic PAP. Between 1999 and 2003, 12 patients elected to receive aerosolised GM-CSF (250 fig b.i.d. every other week) in lieu of whole-lung lavage or observation.

Patient characteristics, pulmonary function tests, arterial blood gas analysis, laboratory values and chest radiographs were extracted from the patient's medical records. Of the six patients tested, all had GM-CSF neutralising antibodies. Additionally, abnormalities in GM-CSF gene expression (one patient), receptor expression (two patients) and ability to upregulate adhesion molecules (one patient) were found.

All patients except one had a positive response (mean improvements in arterial oxygen tension, alveolar-arterial oxygen gradient, carbon monoxide diffusing capacity of the lung and forced vital capacity were 17.1 mmHg, 18.4 mmHg, 16.6% pred and 13.5% pred, respectively). Two patients made a complete recovery and were disease free 1 and 2 yrs after discontinuing treatment. Four patients showed complete response to both the initial course or when treated again for recurrence after discontinuation of treatment. One patient required dose escalation (500 jig b.i.d.) with complete response. GM-CSF was well tolerated without late toxicity after median (range) follow-up of 30.5 (3-68) months.

In conclusion, aerosolised granulocyte-macrophage colony-stimulating factor is safe and effective in treating pulmonary alveolar proteinosis providing an alternative to whole-lung lavage or subcutaneous granulocyte-macrophage colony-stimulating factor.
Descriptors--Author Keywords: granulocyte-macrophage colony-stimulating factor ; pulmonary alveolar proteinosis ; surfactant
Identifiers--KeyWord Plus(R): FACTOR-DEFICIENT MICE; GM-CSF THERAPY; CANCER-PATIENTS; FACTOR-RECEPTOR; LUNG LAVAGE; EXPRESSION; DISEASE; AUTOANTIBODIES; HOMEOSTASIS; PATHOLOGY

Cited References:
JAMA S, 1966, V196, P39
LUKACS NW, 1997, V158, P4478, J IMMUNOL
ANDERSON PM, 1999, V5, P2316, CLIN CANCER RES
BECCARIA M, 2004, V23, P526, EUR RESPIR J
BEWIG B, 2000, V15, P350, EUR RESPIR J
BONFIELD TL, 2002, V105, P342, CLIN IMMUNOL
BONFIELD TL, 2002, V27, P481, AM J RESP CELL MOL
XING Z, 1996, V59, P481, J LEUKOCYTE BIOL
CARBONE DP, 2003, V41, PS103, LUNG CANCER S1
CHEN G, 2003, V284, PL548, AM J PHYSIOL-LUNG C
DENIS M, 1990, V24, P203, IMMUNOL LETT
DEVEGA MG, 2002, V57, P837, THORAX
DIRKSEN U, 1998, V92, P1097, BLOOD
DRANOFF G, 1994, V264, P713, SCIENCE
ESNAULT S, 2001, V21, P117, J INTERF CYTOK RES
HUFFMAN JA, 1996, V97, P649, J CLIN INVEST
IKEGAMI M, 1997, V273, PL709, AM J PHYSIOL-LUNG C
KAVURU MS, 2000, V161, P1143, AM J RESP CRIT CARE
KHWAJA A, 1993, V85, P254, BRIT J HAEMATOL
KITAMURA T, 1999, V190, P875, J EXP MED
KITAMURA T, 2000, V162, P658, AM J RESP CRIT CARE
LADEB S, 1996, V4, P420, SUPPORT CARE CANCER
LIESCHKE GJ, 1994, V84, P27, BLOOD
MONICK MM, 2001, V25, P664, AM J RESP CELL MOL B
NOGEE LM, 1994, V93, P1860, J CLIN INVEST
PALMER LB, 2000, V45, P667, RESP CARE
PRAKASH UBS, 1987, V62, P499, MAYO CLIN PROC
RAGNHAMMAR P, 1994, V84, P4078, BLOOD
REED JA, 1999, V276, P556, AM J PHYSIOL
REED JA, 1998, V110, P321, P ASSOC AM PHYSICIAN
ROSEN SH, 1958, V258, P1123, NEW ENGL J MED
ROSE RM, 1992, V146, P1279, AM REV RESPIR DIS
SANTAMARIA F, 2004, V145, P268, J PEDIATR
SCOTT CL, 1998, V92, P4119, BLOOD
SEYMOUR JF, 2001, V163, P524, AM J RESP CRIT CARE
SEYMOUR JF, 1996, V335, P1924, NEW ENGL J MED
SEYMOUR JF, 2002, V166, P215, AM J RESP CRIT CARE
SEYMOUR JF, 1998, V92, P2657, BLOOD
STANLEY E, 1994, V91, P5592, P NATL ACAD SCI USA
SVENSON M, 1998, V91, P2054, BLOOD
TAKAHASHI K, 2000, V49, P537, CANCER IMMUNOL IMMUN
TAZAWA R, 2005, IN PRESS AM J RESP C
TCHOUWONG KM, 1997, V156, P1999, AM J RESP CRIT CARE
TOMIOKA H, 2004, V10, P3297, CURR PHARM DESIGN
TRAPNELL BC, 2003, V349, P2527, NEW ENGL J MED
UCHIDA K, 2004, V103, P1089, BLOOD
WASSERMAN K, 1968, V44, P611, AM J MED
WYLAM ME, 2000, V161, PA889, AM J RESP CRIT CARE
YAMASHITA N, 2002, V219, P92, CELL IMMUNOL
ZSENGELLER ZK, 1998, V9, P2101, HUM GENE THER

**6/9/15 (Item 2 from file: 34)**
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


11263714 Genuine Article#: 631VN Number of References: 31
**Title: Anti-GM-CSF titer predicts response to GM-CSF therapy in pulmonary alveolar proteinosis**

Author(s): Bonfield TL (REPRINT) ; Kavuru MS; Thomassen MJ
Corporate Source: Cleveland Clin Fdn,Dept Pulm & Crit Care Med,9500 Euclid Ave/Cleveland//OH/44195 (REPRINT); Cleveland Clin Fdn,Dept Pulm & Crit Care Med,Cleveland//OH/44195; Cleveland Clin Fdn,Dept Cell Biol,Cleveland//OH/44195
Journal: CLINICAL IMMUNOLOGY, 2002, V105, N3 (DEC), P342-350
ISSN: 1521-6616 Publication date: 20021200
Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA
Language: English Document Type: ARTICLE
Geographic Location: USA
Journal Subject Category: IMMUNOLOGY
Abstract: Pulmonary alveolar proteinosis (PAP) is an idiopathic disease characterized by the accumulation of surfactant in the pulmonary airspaces. The development of a PAP-like syndrome in the GM-CSF knockout mouse and resolution of disease by local GM-CSF expression strongly implicates GX-CSF in surfactant; homeostasis and disease pathogenesis Based on murine data, GM-CSF therapy was administered to PAP patients, with a subset of response to GM-CSF therapy in some patients is unexplained. In adult idiopathic PAP there appears to be no intrinsic cellular defect in synthesizing or secreting GM-CSF and/or function in the GM CSF receptor subsequent studies have shown the presence of circulating, nentralizing anti-GAI-CSF antibodies in all adult PAP patients studied to date. Whether the anti-GM-CSF is causally related to the PAP disease and whether it should be the target of manipulation remains to be determined. The present study quantified the anti-Gm-CSF levels sequentially in PAP patients receiving GM-CSF therapy. The data indicate that titers of circulating anti-GM-CSF predict response to GH-CSF therapy. In addition, we presenting data from a patient undergoing PlasmaPheresis n which anti-GM-CSF titer decreased with improv these data support the Together in the lung disease, hypothesis that PAP is an anti-GM-CSF autoimmune disease due to the development of antibodies, which results in the deactivation or neutralization of GmCSF. (C) 2002 Elsevier Science (USA).
Identifiers--KeyWord Plus(R): COLONY-STIMULATING FACTOR; FACTOR-DEFICIENT MICE; BETA-C RECEPTOR; PATHOLOGY; DISEASE; CANCER; VALUES; DEFECT
Cited References:
*IMM CORP, 1998, LEUK SARG PACK INS
JAMA-J AM MED ASSOC, 1986, V256, P1333
BARRACLOUGH RM, 2001, V56, P664, THORAX
BEWIG B, 2000, V15, P350, EUR RESPIR J
BUKOWSKI RM, 1993, V13, P267, J IMMUNOTHER
CARRAWAY MS, 2000, V161, P1294, AM J RESP CRIT CARE
CLARK WP, 2002, V131, P453, ANN INTERN MED
CRAPO RO, 1999, V160, P1525, AM J RESP CRIT CARE
DAVIDSON A, 2001, V345, P340, NEW ENGL J MED
DIRKSEN U, 1997, V100, P2211, J CLIN INVEST
DRANOFF G, 1994, V264, P713, SCIENCE
KAVURU MS, 2000, V161, P1143, AM J RESP CRIT CARE
KITAMURA T, 1999, V190, P875, J EXP MED
KITAMURA T, 2000, V162, P658, AM J RESP CRIT CARE
LESILE D, 2001, V108, P1417, J CLIN INVEST
MAZZONE P, 2001, V68, P977, CLEV CLIN J MED
MOKRZYCKI MH, 1994, V23, P817, AM J KIDNEY DIS
NISHINAKAMURA R, 1996, V183, P2657, J EXP MED
REED JA, 1999, V276, PL556, AM J PHYSIOL
SASSE SA, 1994, V106, P187, CHEST
SCHOCH OD, 2002, V57, P277, THORAX
SEYMOUR JF, 1998, V92, P2657, BLOOD
SEYMOUR JF, 1996, V335, P1924, NEW ENGL J MED

SEYMOUR JF, 2001, V163, P523, AM J RESP CRIT CARE
SHAH PL, 2000, V55, P67, THORAX
STANLEY E, 1994, V91, P5592, P NATL ACAD SCI USA
TANAKA N, 1999, V442, P246, FEBS LETT
THEOFILOPOULOS AN, 1979, V28, P89, ADV IMMUNOL
THOMASSEN MJ, 2000, V95, P85, CLIN IMMUNOL
ULLENHAG G, 2001, V99, P65, CLIN IMMUNOL
ZSENGELLER ZK, 1998, V9, P2101, HUM GENE THER

**6/9/16 (Item 3 from file: 34)**

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


10089054 Genuine Article#: 484GB Number of References: 26
**Title: Change in cytokeratin 19 fragment level according to the severity of pulmonary alveolar proteinosis**
Author(s): Minakata Y (REPRINT) ; Kida Y; Nakanishi H; Nishimoto T; Yukawa S
Corporate Source: Wakayama Med Univ,Dept Internal Med 3, Sch Med,811-1 Kimiidera/Wakayama 6410012//Japan/ (REPRINT); Wakayama Med Univ,Dept Internal Med 3, Sch Med,Wakayama 6410012//Japan/
Journal: INTERNAL MEDICINE, 2001, V40, N10 (OCT), P1024-1027
ISSN: 0918-2918 Publication date: 20011000
Publisher: JAPAN SOC INTERNAL MEDICINE, 34-3 3-CHOME HONGO BUNKYO-KU, TOKYO, 113, JAPAN
Language: English Document Type: ARTICLE
Geographic Location: Japan
Journal Subject Category: MEDICINE, GENERAL & INTERNAL
Abstract: A 48-year-old man was diagnosed with primary alveolar proteinosis (PAP). Whole lung lavage was performed for treatment, and the opacity on his chest X-ray completely disappeared. The value of cytokeratin 19 fragment (CYFRA) in the serum was high at the beginning, decreased after lung lavage, and became elevated again when the disease recurred 7 months later. As PAP is thought to be a problem of surfactant secreted from type H pneumocytes, and a cytokeratin is present in the alveolar epithelial tissue, the value of serum CYFRA might be related to the severity of PAP.
Descriptors--Author Keywords: GM-CSF ; CYFRA ; alveolar type II cell
Identifiers--KeyWord Plus(R): COLONY-STIMULATING FACTOR; LUNG-CANCER; CARCINOEMBRYONIC ANTIGEN; DEFICIENT MICE; PATHOLOGY; SERUM; ELEVATION; MARKERS; ASSAY
Cited References:
ASAMOTO H, 1995, V33, P835, NIPPON KYOBU SHIKKAN
BROERS JLV, 1988, V48, P3221, CANCER RES
DRANOFF G, 1994, V264, P713, SCIENCE
FUJISHIMA T, 1995, V62, P317, RESPIRATION
HIRAKATA Y, 1995, V8, P689, EUR RESPIR J
KARIMAN K, 1984, V162, P223, LUNG
KITAMURA T, 1999, V190, P875, J EXP MED
KITAMURA T, 2000, V162, P658, AM J RESP CRIT CARE
KUROKI Y, 1993, V147, P723, AM REV RESPIR DIS
MOLL R, 1982, V31, P11, CELL
NAITO M, 1985, V23, P912, NIPPON KYOBU SHIKKAN
NAKAMURA Y, 1995, V84, P1909, NIPPON NAIKA GAKKAI
NISHINAKAMURA R, 1995, V2, P211, IMMUNITY
ONODERA T, 1983, V139, P245, TOHOKU J EXP MED
OSBORN M, 1982, V31, P303, CELL
PUJOL JL, 1993, V53, P61, CANCER RES
ROBB L, 1995, V92, P9565, P NATL ACAD SCI USA

ROSEN SH, 1958, V258, P1124, NEW ENGL J MED
STANLEY E, 1994, V91, P5592, P NATL ACAD SCI USA
STIEBER P, 1993, V72, P703, CANCER
SUGAMA Y, 1994, V85, P1178, JPN J CANCER RES
TAKADA M, 1995, V71, P160, BRIT J CANCER
TAKANASHI S, 1990, V28, P1006, NIPPON KYOBU SHIKKAN
TANAKA F, 1989, V27, P968, NIPPON KYOBU SHIKKAN
USUI Y, 1992, V31, P422, INTERNAL MED
WRIGHT JR, 1991, V53, P395, ANNU REV PHYSIOL

**6/9/17 (Item 4 from file: 34)**

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


07147994 Genuine Article#: 128AZ Number of References: 61

**Title: Attenuated hematopoietic response to granulocyte-macrophage colony-stimulating factor in patients with acquired pulmonary alveolar proteinosis**

Author(s): Seymour JF (REPRINT) ; Begley CG; Dirksen U; Presneill JJ; Nicola NA; Moore PE; Schoch OD; vanAsperen P; Roth B; Burdach S; Dunn AR

Corporate Source: PETER MACCALLUM CANC INST,LOCKED BAG 1, A BECKETT ST/MELBOURNE/VIC 3000/AUSTRALIA/ (REPRINT); LUDWIG INST CANC RES,/PARKVILLE/VIC/AUSTRALIA/; ROTARY BONE MARROW RES LABS,/PARKVILLE/VIC/AUSTRALIA/; UNIV DUSSELDORF,MED CTR, DEPT PEDIAT HEMATOL ONCOL/D-4000 DUSSELDORF//GERMANY/; ROYAL MELBOURNE HOSP,DEPT CLIN HAEMATOL & MED ONCOL/PARKVILLE/VIC 3050/AUSTRALIA/; ROYAL MELBOURNE HOSP,INTENS CARE UNIT/PARKVILLE/VIC 3050/AUSTRALIA/; WALTER & ELIZA HALL INST MED RES,/PARKVILLE/VIC/AUSTRALIA/; CHILDRENS HOSP,DIV RESP MED/BOSTON//MA/; UNIV ZURICH HOSP,DIV PULM/CH-8091 ZURICH//SWITZERLAND/; ROYAL ALEXANDRA HOSP CHILDREN,/WESTMEAD/NSW/AUSTRALIA/; UNIV COLOGNE,DEPT PEDIAT/COLOGNE//GERMANY/

Journal: BLOOD, 1998, V92, N8 (OCT 15), P2657-2667
ISSN: 0006-4971 Publication date: 19981015
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: ARTICLE
Geographic Location: AUSTRALIA; GERMANY; USA; SWITZERLAND
Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: HEMATOLOGY

Abstract: The pathogenesis of acquired pulmonary alveolar proteinosis (PAP), a rare lung disease characterized by excessive surfactant accumulation within the alveolar space, remains obscure. Gene-targeted mice lacking the hematopoietic growth factor granulocyte-macrophage colony-stimulating factor (GM-CSF) or the signal-transducing beta-common chain of the GM-CSF receptor have impaired surfactant clearance and pulmonary pathology resembling human PAP. We therefore investigated the hematopoietic effects of GM-CSF in patients with PAP. The hematologic response of 5 infants with congenital PAP to 5 mu g/kg/d was of normal magnitude. By contrast, despite normal expression of GM-CSF receptor alpha- and beta-common chains on peripheral blood myelomonocytic cells (n = 6) and normal binding affinity of bone marrow mononuclear cells for GM-CSF (n = 3), each of the 12 patients with acquired PAP treated displayed impaired responses to GM-CSF; 5 mu g/kg/d produced only minor eosinophilia, and doses of 7.5 to 20 mu g/kg were required to induce greater than or equal to 1.5-fold neutrophil increments in the 3 patients who underwent dose-escalation. However,

neutrophilic responses to 5 mu g/kg granulocyte colony-stimulating factor (G-CSF) were normal (n = 4), In vitro, the proportion of hematopoietic progenitors responsive to GM-CSF (16.1% +/- 8.9%; P = .042) or interleukin-3 (IL-3: 19.3% +/- 7.7%; P = .063), both of which utilize the beta-common chain of the GM-CSF receptor complex, were reduced among patients with acquired PAP (n = 4) compared with normal bone marrow donor controls (47.2% +/- 25.9% and 40.9% +/- 18.6%, respectively). In the one individual who had complete resolution of lung disease during the period of study, this was temporally associated with correction of this defective in vitro response to GM-CSF and IL-3 on serial assessment. These data establish that patients with acquired PAP have an associated impaired responsiveness to GM-CSF that is potentially pathogenic in the development of their lung disease. Based on these observations, we propose a model of the pathogenesis of acquired PAP that suggests the disease arises as a consequence of an acquired clonal disorder within the hematopoietic progenitor cell compartment. (C) 1998 by The American Society of Hematology.

Identifiers--KeyWord Plus(R): RECEPTOR-DEFICIENT MICE; COMMON BETA-CHAIN; FACTOR GM-CSF; ADVANCED MALIGNANCY; PROGENITOR CELLS; GENE-EXPRESSION; STEM-CELLS; IN-VITRO; PHASE-I; CANCER

Cited References:

ARMITAGE P, 1994, STAT METHODS MED RES
BEGLEY CG, 1996, P59, CELL THERAPY
BERTHAUD P, 1993, V80, P418, B CANCER
BROCK TG, 1996, V156, P2522, J IMMUNOL
BUKOWSKI RM, 1993, V13, P267, J IMMUNOTHER
BURGESS AW, 1977, V252, P1998, J BIOL CHEM
CAIRO MS, 1995, V86, P2509, BLOOD
CANNISTRA SA, 1990, V87, P93, P NATL ACAD SCI USA
CHEN GH, 1994, V152, P724, J IMMUNOL
DALE DC, 1998, V57, P7, AM J HEMATOL
DELUCA E, 1992, V66, P893, BRIT J CANCER
DIPERSIO J, 1988, V263, P1834, J BIOL CHEM
DIRKSEN U, 1997, V100, P2211, J CLIN INVEST
DRANOFF G, 1994, V264, P713, SCIENCE
FELDMAN GM, 1997, V90, P1768, BLOOD
GONZALEZROTHI RJ, 1986, V90, P656, CHEST
GOUGH NM, 1984, V309, P763, NATURE
HAAS R, 1990, V18, P94, EXP HEMATOL
HIBBS ML, 1995, V83, P301, CELL
HUFFMAN JA, 1996, V97, P649, J CLIN INVEST
IHLE JN, 1995, V11, P69, TRENDS GENET
IKEGAMI M, 1996, V270, PL650, AM J PHYSIOL
KERST JM, 1993, V82, P3265, BLOOD
LADEB S, 1996, V4, P420, SUPPORT CARE CANCER
LAIRD PW, 1993, V21, P4750, NUCLEIC ACIDS RES
LIESCHKE GJ, 1989, V110, P357, ANN INTERN MED
LIESCHKE GJ, 1992, V327, P28, NEW ENGL J MED
LIU X, 1997, V11, P179, GENE DEV
LORD BI, 1992, V50, P26, INT J CANCER
MATTHEWS JNS, 1990, V300, P230, BRIT MED J
METCALF D, 1995, HEMOPOIETIC COLONIES
MILLER AB, 1981, V47, P207, CANCER
MIYAJIMA A, 1993, V82, P1960, BLOOD
MUNSON PJ, 1980, V107, P220, ANAL BIOCHEM
NICOLA NA, 1992, V6, P119, GROWTH FACTORS
NISHINAKAMURA R, 1995, V2, P211, IMMUNITY
NISHINAKAMURA R, 1996, V183, P2657, J EXP MED
NOGEE LM, 1997, V111, PS129, CHEST S2
NUGENT KM, 1983, V127, P780, AM REV RESPIR DIS

PARKER LA, 1997, V111, P1457, CHEST
QUELLE FW, 1994, V14, P4335, MOL CELL BIOL
RAGNHAMMAR P, 1994, V84, P4078, BLOOD
ROBB L, 1995, V92, P9565, P NATL ACAD SCI USA
ROSEN SH, 1958, V258, P1123, NEW ENGL J MED
SEYMOUR JF, 1996, V335, P1924, NEW ENGL J MED
SMITH A, 1997, V16, P451, EMBO J
STAHL N, 1993, V74, P587, CELL
STANLEY E, 1994, V91, P5592, P NATL ACAD SCI USA
STEWARD WP, 1990, V61, P749, BRIT J CANCER
THOMAS ED, 1976, V192, P1016, SCIENCE
THOMASSEN MJ, 1989, V49, P4086, CANCER RES
UDY GB, 1997, V94, P7239, P NATL ACAD SCI USA
UEDA T, 1995, V268, PL363, AM J PHYSIOL
VADHANRAJ S, 1988, V72, P134, BLOOD
VADHANRAJ S, 1992, V10, P1266, J CLIN ONCOL
WADHWA M, 1996, V104, P351, CLIN EXP IMMUNOL
WASSERMAN K, 1994, P1933, TXB RESPIRATORY MED
WATANABE S, 1996, V271, P12681, J BIOL CHEM
WRIGHT JR, 1990, V259, PL1, AM J PHYSIOL
ZHANG R, 1994, V91, P12755, P NATL ACAD SCI USA
ZMUIDZINAS A, 1995, V14, P1, EMBO J

**6/9/18 (Item 5 from file: 34)**

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


03729247 Genuine Article#: QA899 Number of References: 16

**Title: A NOVEL, SIMPLE, RELIABLE, AND SENSITIVE METHOD FOR MULTIPLE IMMUNOENZYME STAINING - USE OF MICROWAVE-OVEN HEATING TO BLOCK ANTIBODY CROSS-REACTIVITY AND RETRIEVE ANTIGENS**

Author(s): LAN HY; MU W; NIKOLICPATERSON DJ; ATKINS RC
Corporate Source: MONASH MED CTR,DEPT NEPHROL,246 CLAYTON RD/CLAYTON/VIC 3168/AUSTRALIA/

Journal: JOURNAL OF HISTOCHEMISTRY & CYTOCHEMISTRY, 1995, V43, N1 (JAN), P 97-102
ISSN: 0022-1554
Language: ENGLISH Document Type: NOTE
Geographic Location: AUSTRALIA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: CELL BIOLOGY

Abstract: We report a simple and reliable method for detection of two or more antigens within tissue sections by indirect immunoenzyme staining using mouse monoclonal antibodies (MAbs). This technique involves treating sections with two 5-min microwave (MW) oven heatings between sequential rounds of three-layer immunoenzyme staining (mouse MAb, goat anti-mouse IgG, and mouse PAP or mouse APAAP) and color development. Discrete staining of cell surface, cytoplasmic, and nuclear antigens was evident within individual cells. This technique has a number of advantages over those currently available. First, MW treatment denatures bound antibody molecules, thereby completely blocking crossreactivity between sequential rounds of staining. This allows the use of primary (and other) antibodies raised in the same species and the use of a sensitive three-layer staining method. Second, antigen retrieval after MW treatment markedly increases the sensitivity of cytoplasmic and nuclear antigen detection. Third, inactivation of peroxidase and alkaline phosphatase enzymes present in PAP and APAAP complexes prevents inappropriate color development. Finally, this method can be used in both paraformaldehyde-fixed cryostat sections and

formalin-fixed paraffin tissue sections. In conclusion, this is a simple, reliable, and sensitive technique that will be useful in many areas of diagnosis and research.

Descriptors--Author Keywords: MULTIPLE IMMUNOENZYME STAINING ; MICROWAVE ; ANTIBODY DENATURATION ; ANTIGEN RETRIEVAL ; LEUKOCYTE ; PROLIFERATION

Identifiers--KeyWords Plus: MONOCLONAL-ANTIBODIES; TISSUE-SECTIONS; RECEPTOR

Research Fronts: 93-2411 001 (RAT MICROGLIAL CELLS; CYTOKINE EXPRESSION OF MACROPHAGES; CULTURED ASTROCYTES; AUTOIMMUNE POTENTIAL; NEUROLOGICAL DISEASE; DIFFERENTIAL INDUCTION)

93-2612 001 (MALIGNANT FIBROUS HISTIOCYTOMA; GIANT-CELL TUMORS; PRIMARY RHABDOMYOSARCOMA; MACROPHAGE IMMUNOPHENOTYPE; CLINICOPATHOLOGICAL FEATURES; GM-CSF M-CSF)

93-3155 001 (PROLIFERATING CELL NUCLEAR ANTIGEN; PROGNOSTIC IMPACT IN ARCHIVAL PARAFFIN-EMBEDDED NODE-NEGATIVE BREAST-CANCER; IMMUNOHISTOCHEMICAL EVIDENCE)

93-3816 001 (KI-67 ANTIGEN; P53-PROTEIN EXPRESSION; FIXED PROLIFERATING CELLS; IMMUNOHISTOLOGICAL DETECTION; MICROWAVES IN IMMUNOHISTOCHEMICAL TECHNIQUES)

Cited References:

BOORSMA DM, 1984, V80, P103, HISTOCHEMISTRY
CARL SAL, 1993, V41, P1273, J HISTOCHEM CYTOCHEM
CLAASSEN E, 1986, V34, P423, J HISTOCHEM CYTOCHEM
DIJKSTRA CD, 1985, V54, P589, IMMUNOLOGY
HUING T, 1989, V169, P73, J EXP MED
KUNG PC, 1979, V206, P347, SCIENCE
LAN HY, 1993, V43, P479, KIDNEY INT
MASON JT, 1991, V39, P225, J HISTOCHEM CYTOCHEM
PULFORD KAF, 1989, V42, P414, J CLIN PATHOL
SHI SR, 1991, V39, P741, J HISTOCHEM CYTOCHEM
SHI SR, 1993, V41, P1599, J HISTOCHEM CYTOCHEM
SUNDERLAND CA, 1979, V9, P155, EUR J IMMUNOL
TIDMAN N, 1981, V45, P457, CLIN EXP IMMUNOL
VANDERLOOS CM, 1987, V35, P1199, J HISTOCHEM CYTOCHEM
VANROOIJEN N, 1985, V33, P175, J HISTOCHEM CYTOCHEM
WASEEM NH, 1990, V96, P121, J CELL SCI

?